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The Edward Stirling Lectures.[1]

LECTURE II: THE SARCOMATA OF BONE.[2]

By R. KAYE SCOTT M.D., M.S. (Melbourne), F.R.A.C.S., F.F.R., F.C.R.A., D.T.R.E. (Melbourne),
Melbourne.

IN any discussion of tumours of bone it is essential to have before us a reasonable classification for clinical use.

The classification accepted by the American Registry in 1939 and still official is as follows:

1. *Osteogenic series*:
   Osteogenic sarcoma: Malignant: (i) medullary and subperiosteal, (ii) telangiectatic, (iii) sclerosing (iv) periosteal, (v) fibrosarcoma—(*a*) medullary, (*b*) periosteal—(vi) parosteal, capsular. Benign: (i) exostosis, (ii) osteoma.
2. *Chondroma series*:
   Malignant: (i) chondrosarcoma, (ii) myxosarcoma. Benign: (i) chondroma.
3. *Giant-cell tumour series*:
   Malignant. Benign: (i) epiphyseal giant-cell tumour.
4. *Angioma series*:
   Malignant: (i) angioendothelioma, (ii) diffuse endothelioma. Benign: (i) cavernous angioma, (ii) plexiform angioma.
5. *Myeloma series*:
   Malignant: (i) plasma cell, (ii) myelocytoma, (iii) erythroblastoma.
6. *Reticulum-cell lymphosarcoma.*
7. *Liposarcoma.*

For clinical purposes it is possible to simplify the American Registry classification, which includes certain subgroups that are now outmoded. In the classification it is necessary to show only the broad groups which are encountered; it is only confusing at this stage to indicate the pathological and radiological subgroups. The following classification is therefore offered:

IA. *Osteogenic Sarcoma.*

(i) Osteocyte series:
Undifferentiated osteolytic type.
Intermediate type with some bone or cartilage formation.
Sclerosing or osteosarcoma.
Innocent counterparts: osteoma and subgroups.

(ii) Chondrocyte series:
Primary and secondary chondrosarcoma (differentiated and undifferentiated types).
Innocent counterparts: Chondroma and subgroups.
Chondroblastoma—malignant.
Innocent counterpart: Chondroblastoma—benign.

[1] Delivered on May 31 and June 2, 1955, at Adelaide.

[2] Dr. Kaye Scott illustrated his lecture with lantern slides showing photomicrographs of histological sections, clinical photographs and reproductions of X-ray films of illustrative patients.

(iii) Fibrocyte series:
Fibrosarcoma.
Innocent counterparts: Fibroma—ossifying and non-ossifying.

Ib. *Giant-cell Tumours.*
Osteoclast series:
Giant-cell tumour—malignant.
Innocent counterpart: Giant-cell tumour—benign.

II. *Reticulo-endothelial Tumours in Bone.*
A. Marrow series: Solitary and multiple myeloma, chloroma.
B. Reticulum-cell series: Hodgkin's disease, reticulum-cell sarcoma.
C. Lymphocytic cell series: lymphosarcoma.
D. Endothelial cell series: (*a*) angioma of bone, (*b*) endothelioma (?) of bone (Ewing's tumour if primary).

III. *Epithelial Organoid Tumours of Bone.*
A. Alveolar odontomes: (i) epithelial (adamantinoma) group; (ii) mixed, producing tooth structures; (iii) mesenchymal.
B. Adamantinoma in other sites: tibia, Rathke's pouch, *et cetera.*

Two great tissues comprise bone — bone proper and marrow. Bone proper is the most adult form of connective tissue represented in the series myxomatous connective tissue, fibrous connective tissue, cartilage and bone. The adult parenchymatous cells of bone are the osteocyte and the osteoclast. The osteocyte is derived from the osteoblast, which in turn comes from primitive mesenchyme. From the same source comes the osteoclast, and Willis stresses the fact that the osteoclast does not appear as a cell of a continuing tissue, but that it is formed as required from the mesenchyme and actually may be interchangeable with the osteoblast, the difference between the two cells perhaps being due to different enzymic production referable to the functional activities in hand. Tumours from these cells form two great subdivisions of the first group of parenchymatous primary bone tumours: the osteoma and osteogenic sarcoma series on the one hand, and the giant-cell tumours, innocent and malignant, on the other hand.

"Osteogenic" is a bad adjective for use in describing the group. It implies "bone forming", but is used otherwise to imply that the tumour arises from tissues normally having bone-forming capacity—a property which may not be exhibited by a tumour derived from that tissue. Thus a wide range of tumours is included in the osteogenic sarcoma group, which contains some neoplasms showing bone or osteoid production and others exhibiting cartilage formation, while still others are of fibroid or myxoid type in whole or in part. The degree of differentiation exhibited depends on the potentialties of the tissues of origin. These may be related to age of onset and site of origin.

If the tissue of origin has capacity for differentiation and the environment is suitable, a bone-forming sclerotic tumour results. If an undifferentiated tumour is produced, no bone or cartilage is present. Intermediate types occur, but very often individual tumours are found to show varying degrees of differentiation and undifferentiation.

Cartilage-containing tumours if arising *de novo* are referred to as primary chondrosarcomata; others commencing in preexisting cartilaginous tumours of innocent type or in rests of chondroblastic tissue, are referred to as secondary chondrosarcomata.

The chondroblastoma group comprises a recently recognized tumour entity appearing in the site of the epiphyseal line and composed of primitive cells having potentiality for formation of cartilage. Chondroblastoma has in the past been confused both radiologically and histologically with the giant-cell tumour. Most of the tumours are innocent; some authorities describe a malignant variety.

A pure fibrosarcoma occurs in bone and shows a typical spindle-cell structure with formation of an intercellular collagenous matrix which may contain mucin. It has no tendency to form bone. Similarly, a non-ossifying fibroma of bone has been described; but it becomes difficult to separate such an entity from such a condition as localized *osteitis fibrosa.*

These non-ossifying tumours must be supposed to originate from the primitive mesenchyme which forms the original cartilaginous skeleton. This mesenchyme becomes specialized to form chondroblast, osteoblast or osteoclast, some fibroid cells persist as periosteum or endosteum, so there is no reason why a non-ossifying fibroid tumour should not arise in tissue of such diverse potentiality.

The giant-cell tumour has posed problems ever since its recognition. All the evidence now available points to the tumefaction's being an osteoclastoma; some authorities hold that the osteoclast is but a phagocyte and the condition may be a hyperplastic inflammatory one, but in general the giant-cell tumour is accepted as a neoplasm. However, further argument rages about the alleged malignant variety; Geschicter and Copeland (1949) place it among their lytic group of osteogenic sarcomata. In this country its authenticity is generally accepted, in accordance with the teaching of King.

Tumours arising primarily in bone marrow constitute another great group legitimately placed among true tumours of bone. Marrow is a tissue of reticulo-endothelial origin; it forms an essential part of the reticulo-endothelial system and becomes specially differentiated to form circulating cells of the erythrocytic, granular and platelet series. There is no sharp line between hyperplastic dyscrasias of marrow and some of the tumours of marrow, and all can legitimately be included in a classification of the reticuloses. The localized tumefactions, as opposed to the diffuse hyperplasias of marrow, can be included among the tumours of bone.

The reticulo-endothelial cell has a remarkable capacity for pleomorphic differentiation; the primitive reticulo-endothelial cell in the lymph gland forms cells of the reticulum series, the lymphocytic series and the endothelial series. But, for example, in the gland under conditions of disease, abnormal formation of blood cells may occur. Similarly, in bone marrow we may see abnormal differentiation of the primitive reticulo-endothelial cell. Single and multiple forms of marrow tumours are seen as plasmacytoma and multiple myeloma respectively, while chloroma is another member of the same family, all members of which merge imperceptibly into the leuchæmia-polycythæmia-megakaryocytosis group.

Under conditions of disease, hyperplastic processes of the reticulum cell may be seen as Hodgkin's disease of bone marrow or as a real reticulum-cell sarcoma of bone.

If Ewing's tumour is regarded as an endothelioma, then it should be included here among the reticuloses of bone; otherwise it must be regarded as a secondary neuroblastoma of bone.

The third great group of primary bone tumours includes the adamantinoma group, and these are organoid tumours of bone and epithelium, though one tissue may outgrow another. The mandibular and maxillary alveoli are peculiar among bones because of the presence of the dental ridge downgrowths of epithelium which form teeth structures. Thus a whole series of primary tumours involving bone occurs, forming the odontomes, which may be classified as follows: (*a*) mixed odontomes containing epithelial and mesenchymal structures, producing tooth formations; (*b*) epithelial odontomes containing chiefly epithelial structures, varying from the simple cystic epithelial odontome through epithelioma to adamantinoma; (*c*) the mesenchymal odontome, which contains only connective-tissue structures.

Adamantinoma may occur as a primary bone tumour in other sites, as, for example, in the tibia, where the epithelial appearances continue to present pathological puzzles. Hicks (1954) has suggested that the tibial adamantinoma is really a synovial sarcoma. In other places, like the Rathke pouch tumours, the presence of epithelium in the bone is well understood.

Little is known of any cause for the production of an osteogenic sarcoma, and while trauma is often an incident in the history there is little to blame injury as being a real ætiological factor. Examination of the clinical material shows that the tumours arise in the great majority of

cases as manifestations of an abnormality of growth at a place and time where normal growth is an active process. Most of the juvenile osteogenic sarcomata are accounted for in this fashion; the later group occurring in early middle age are more often chondrosarcomata, in which growth occurs in a tissue rest. In the late age group osteogenic sarcoma may occur in Paget's disease, in which great resorption and activity are occurring in the bone.

The tissue of origin is apparently some part of the primitive mesenchyme which forms the condensation representing the embryonic bone. This is soon formed into a cartilaginous mass, and the aggregation of mesenchyme around it becomes the perichondrium and later the periosteum. In the adult only a very small fraction of the shaft is represented by the original embryonic diaphysis; most of the adult shaft is formed by epiphyseal growth. In these processes we see original mesenchymal cells forming chondrocytes, and later osteoblasts and osteoclasts are formed as occasion demands. The potentialities of the primitive mesenchyme are thus illustrated, and this mesenchyme is represented in the adult as simple fibrous connective tissue in periosteum and endosteum; from this tissue at any time can be formed osteoblasts, osteoclasts or other varieties of cells. Under conditions of abnormal growth tumours derived from these tissues appear as undifferentiated forms; some have metaplastic capacity and produce adult tissues. There will therefore be nothing abnormal in the appearance of immature osteoblasts, chondroblasts or fibroblasts in the tumours. The pleomorphic stumpy-tailed cell with the dense chromatin-filled nucleus represents the osteoblast; but under another guise there may appear the spindle cell of fibrous-tissue type representing the return to the primitive mesenchyme.

One must not think so much of an adult osteoblast becoming malignant and forming bone, osteoid or cartilage. It is more likely that a much more primitive group of cells derived from the endosteal or periosteal representations of the original mesenchyme undergoes proliferation. These cells may have sufficient metaplastic potentiality to develop bone or cartilage; alternatively, only non-ossifying fibrosarcomatous tissue may be formed.

In the cartilage bones the osteoblast lays down the adult bone under the epiphyseal line. Cartilage is being continually formed in the epiphysis, and calcification takes place within this cartilage. At the epiphyseal line the osteoclasts destroy the calcified cartilage and apparently make available to the osteoblasts the calcium and phosphorus, so that the osteoblasts directly lay down new bone of cancellous type.

Osteoblasts in the inner layer of the periosteum are laying down new bone directly, but here without a prior stage of calcified cartilage. Exactly the same process occurs in membrane bones, where the fibrous type of connective tissue cells directly lay down the permanent bone.

Therefore, it is most natural that as a manifestation of undifferentiation in an osteogenic sarcoma either the fibroid or the osteoblastic type of cells may appear.

Price (1952) reported a study in which he attempted to grade on histological appearances a series of osteogenic sarcomata according to their degree of malignancy. He found that the cell in 80% of his cases was of osteoblast type and in 20% was of spindle or fusiform type representing the fibroblast.

Diagnosis of the Early Sarcoma of Bone.

Clinical methods alone have proved inadequate in the diagnosis of bone tumours, and neither radiological nor histological examination is capable of returning universally accurate answers.

A history of trauma in 20% to 50% of cases may serve only to draw attention to the pathological process made manifest by pain, swelling and limitation of movement. In about one-fifth of the established cases constitutional symptoms of fever and leucocytosis may be present — a finding, therefore, not exclusive to Ewing's syndrome.

The radiologist can give a definite diagnosis in the well-established sclerotic osteosarcoma, but in many an early case of lytic sarcoma with a limited area of bone destruction, and in the absence of tumour, bone or calcification or with little periosteal reactive change, diagnosis is extremely difficult and accurate diagnosis an impossibility. Yet in such an early case is a definite answer imperative, for chance of cure depends so much on early and appropriate action. Biopsy therefore becomes essential. It must not be undertaken lightly. The osteogenic sarcoma does find itself limited by the barriers of the tissue planes it encounters; the epiphyseal plate resists it, it pushes periosteum outwards in successive stages before it breaks through it, the planes of muscle and fascia and subcutaneous tissue all bulge long before they are infiltrated.

Incision through the centre of such a mass for biopsy purposes has been seen only too often; fungation through the biopsy wound follows too frequently.

Geschicter and Copeland (1949) state that "all forms of osteogenic sarcoma are aided in their spread and invasive tendencies by partial excision or incision".

Biopsy should be performed only if the radiologist is unable to give an absolutely certain diagnosis. It should be done in the first instance by aspiration technique. An electric motor on a type of dental drill holder is fitted with a tubular cutter one-eighth of an inch in diameter, with sharpened edges, and this will obtain most readily a sizeable fragment for pathological examination without undue tissue damage through a minute puncture. If the bone is dense, a hand drill is used with a toothed cutting bit. The skin stab is made from the side of the tumour and never directly over the swelling.

Alternatively Geschicter and Copeland advise that open biopsy should be performed on the operating table, with an operation team prepared to go on to amputation after the pathologist has examined a frozen section. However, in this difficulties may arise, for frozen sections are not always easy of interpretation and immediate treatment may not be the best treatment. An alternative is to administer preliminary X-ray therapy in suitable cases and take a drill biopsy after a few weeks of treatment.

Clinical Varieties of Osteogenic Sarcoma.

Willis (1948) states that he is opposed to the subdivision of primary tumours of bone beyond those groups barely necessary, and thinks that even the main divisions lack histogenetic significance. This point is clearly brought out by Price (1952, *vide supra*), who found that neither the type of cell nor the variety of matrix produced provided any reliable guide to the malignancy of the tumour. He decided that the ratio between the number of mitoses observed and the number of resting nuclei present formed the only adequate indication of the malignancy of the tumour.

The official American Registry classification describes *inter alia* "medullary and subperiosteal", "telangiectatic", "sclerosing", "periosteal" and "fibrosarcomatous" types. These terms are in part anatomical, in part pathological, in part descriptive, and their use is no longer countenanced.

The recent books on bone tumours describe in great histological detail numerous varieties of these tumours. For practical purposes it is sufficient for the radiologist and the clinician to use a very few descriptive headings and report osteosarcoma if obvious new bone is present, chondrosarcoma if calcification or loculation indicates it, osteolytic osteogenic sarcoma if a destructive soft-tissue mass is present.

So few cases are seen per year, and the prognosis in the different varieties differs so little, that nothing is gained by further subdivision in ordinary practice. But in those departments which have the handling of these patients it is profitable to examine them a little more closely, when it is found that the tumours do fall into a reasonably small number of subgroups. These are by no means clear-cut subdivisions, and this lends point to Willis's argument. Subgroups may be made according to histogenesis and capacity for differentiation, and site of tumour origin.

The Osteosarcoma Group.

The undifferentiated tumour arising from primitive mesenchymal tissue of bone-forming potentiality is seen as a destructive neoplasm arising in the region of the metaphysis in young subjects. The tumour commences centrally in the site of most active normal bone production. It quickly causes erosion of medullary and cortical bone and forms a huge soft-tissue mass, causing ballooning of the region and infiltrating widely. There is no periosteal reaction whatever, and the ragged end of the shaft of the bone projects into the tumour, which usually completely destroys both epiphyseal and metaphyseal portions of the bone.

Undifferentiated tumours may show metaplastic tendencies by the attempted formation of cartilage or bone. A neoplasm with these characteristics represents an intermediate type between the undifferentiated osteogenic sarcoma and the highly differentiated bone-producing osteosarcoma.

The bone-productive sarcoma, called the "sclerosing" sarcoma or, better, plain "osteosarcoma", has origin in three common sites, all of which are again sites of active bone production in the growing individual. The undifferentiated type arises centrally, the differentiated types appear in subperiosteal situations. In the long bones the sclerosing tumours appear either along the shaft or, secondly, below the periosteum of the metaphysis adjacent to the epiphyseal line; thirdly, they may appear in membrane bones.

In the shaft of long bones the tumour quickly elevates the periosteum and tends to grow both around the shaft and up and down along its length. But also invasion of cortex and medulla occurs quickly, and the tumour, because of its capacity for differentiation, early commences the deposition of neoplastic bone both in the soft tumour mass and in the invaded shaft. At the commencement of growth it may be difficult to recognize this tumour type, because tumour bone formation must be differentiated from periosteal reactive phenomena and calcification in a chondroid tumour. "Sunrays" under an elevated periosteum are caused by deposition of bone by normal osteoblasts alongside vessels running between the elevated periosteum and the remaining cortex; "onion skin" is similarly due to activity of normal subperiosteal osteoblasts. Production of bone from these two sources is a rapid response to periosteal stripping from any cause, whether inflammation, hæmatoma or tumour, and so would tend to appear before neoplastic bone formation.

In general, subperiosteal depositions which run longitudinally are easily recognized, and the transverse sunrays of periosteal reactive type are fine, while tumour bone is a most coarse deposition because it is laid down *en masse*. One further major difficulty arises because of circumferential tumour spread. Subperiosteal depositions lying in front of or behind the shaft may appear to be within the cortex, particularly if the deposition is dense. It is important to determine whether the medulla is invaded and sclerosed, for this is a constant finding in the osteosarcomata, while in the diaphyseal and juxtaepiphyseal types of chondrosarcoma medullary sclerosis is absent. The tumour bone runs outwards in coarse irregular trabeculæ at right angles to the length of the shaft, and ossification commences near the cortical surface.

The osteosarcoma commencing in the juxtaepiphyseal situation is seen early as a subperiosteal tumefaction, with raised periosteum and cortical destruction. Reactive phenomena of sunrays and subperiosteal bone deposition appear early, tumour sclerosis occurs later and produces dense shadows around the shaft and ultimately sclerosis of the medulla. The tumour commences subperiosteally in the metaphyseal region, which is a site of active periosteal bone deposition at the age of tumour occurrence. The osteoblastic parenchyma progresses directly to dense bone formation without any stage of cartilage formation.

Sarcomata in the membrane bones are rare of appearance, and both sclerosing types and undifferentiated osteolytic varieties are seen. It must be emphasized that actual deposition of bone in both cartilage and membrane bones is essentially the same process—in the membrane bone the osteoblast directly lays down bone exactly as does the osteoblast lying under the epiphysis. The prior calcification in cartilage with osteoclastic mobilization of calcium and phosphorus storage reserves assists osteoblastic deposition of medullary trabeculæ in long bones. This is a mechanism associated with the greatly increased growth necessities of the long as opposed to the membrane bones.

The Chondrosarcoma Group.

Chondrosarcomata are arbitrarily divided into two groups, primary and secondary. Secondary tumours arise in association with a preexisting chondroma or cartilaginous remnant, and so appear generally in middle-aged people; the primary chondrosarcomata arise in the juvenile age group from primitive mesenchyme with potentiality for forming cartilage.

The primary tumours occur in the same two sites in long bones as do the osteosarcomata, and in the flat bones chondrosarcomata constitute an additional important group of tumours. Rarely they occur in membrane bones; for example, a chondrosarcoma of the mandible is a definite entity.

A subperiosteal chondrosarcoma occurring in the midshaft region of long bones probably arises in tissue representing the perichondrium originally lying around the infantile cartilaginous shaft.

Near the epiphysis the tumour is said to arise on the tuberosities, and this is one of the commonest forms of osteogenic sarcoma—originally described as the "medullary and subperiosteal type".

The tumour mass is formed essentially of undifferentiated cells, though wide areas of well-developed cartilage appear in some tumours, and all transitions may be seen between the two extremes. Periosteal reactive phenomena are prominent and may too readily suggest an erroneous classification into the osteosarcoma group. Cortical destruction is seen early, but there is no intramedullary sclerosis. Lagging well behind the soft-tissue invasion may come calcification within the tumour. This is granular and blotchy, and is separated from the cortex by areas of uncalcified tumour, a consequence of its focal deposition. However, the calcification may sometimes be so dense that differentiation of the osteosarcoma and chondrosarcoma groups is difficult.

A primary undifferentiated variety of chondrosarcoma may arise in flat bones in young people; the sternum is a classical site. A huge outgrowth tumour has been seen in a boy; it grew to a size of six inches in diameter in a period of three months. It then ulcerated and fungated and caused rapid death from secondary deposits in the lungs.

Secondary chondrosarcomata are those tumours which arise in association with a demonstrable and previously existing portion of abnormal cartilage. Such neoplasms may arise in a simple bone spur of osteochondromatous type, more commonly in the growing masses of abnormal cartilage which constitute ossifying chondromata in long and flat bones. These are all enchondromata—that is, cartilaginous tumefactions appearing in sites in which cartilage should not remain in the adult. In some sites like the metacarpals, enchondromata remain as innocent tumours; in the sternum malignant change occurs readily. In the pelvis many ossifying chondromata will remain localized for long periods of years, but any interference or incomplete removal is disastrous.

In the first instance a non-ossified, often lobulated cartilaginous mass replaces some normal bone. Loculi and calcification are the two great radiological indications of a central chondroma. The further lytic destruction of normal bone occurring around the original chondroma may make it difficult to be certain that a chondroma did in fact preexist; the presence of irregular calcification is often the only remaining evidence.

The chondroblastomatous tumour group has been recognized as a separate clinical entity among radiotherapists for many years—particularly those tumours of the humerus in children, the cartilaginous nature of which was well recognized after Codman's description in 1931. But only in

the last ten years, since the work of Jaffe and Lichenstein (1942), has the pathology been understood; even now complete unanimity has not been attained.

In the epiphyses there is normally a great production of cartilage, which becomes calcified just above the epiphyseal line. The chondroblastoma is composed of an abnormal growth of embryonic cartilage cells filling the epiphyseal region and extending down the shaft from an abnormal epiphyseal line. The embryonic cartilage cells do not produce an adult cartilaginous matrix which calcifies normally. Hence there is no regular epiphyseal line with orderly osteoclastic cartilage resorption and osteoblastic deposition of medullary bone. A disordered mass of primitive tumour cartilage extends down the shaft, with masses of giant cells of osteoclastic type at its edges. These osteoclasts are most likely cells of normal type attempting only a normal job, but become hyperplastic because they encounter abnormal cartilaginous matrix.

Thus the tumour has been mistaken for a giant-cell tumour or a mixed giant-cell and cartilaginous tumour. Osteoblastic deposition of cancellous bone simply does not occur, and a long zone beneath the growing epiphysis is filled with a mass of embryonic cartilage and giant-cell tissue. Radiologically the trabeculation below the epiphysis has often been mistaken for the simple giant-cell tumour; however, the loculation of cartilage is always discernible and allows the diagnosis to be made with confidence.

Argument still rages as to whether a malignant form of the tumour exists. Lichenstein (1952) does not admit a malignant variety. Geschicter and Copeland (1952) describe a malignant variant.

Fibrosarcoma of Bone.

Fibrosarcoma of bone is a destructive and lytic tumour most commonly occurring in the metaphysis in young people. There is a much rarer fibrosarcoma occurring in association with the periosteum sometimes referred to as a parosteal sarcoma. The essential feature of all these tumours is their fibroid character, as opposed to a composition of cells of undifferentiated osteoblast type. The cells are of spindle type with elongated nuclei; they form intercellular fibrils of hyalin or collagen, sometimes intercellular mucin, but under no circumstances is there formation of cartilage or bone.

Radiologically, therefore, the tumours are essentially lytic in type, arising eccentrically in the metaphysis, eroding medulla and cortex, sometimes multiloculated, sometimes showing coarse residual trabeculæ of bone. The tumour readily invades adjacent soft tissue or joint cavity and large swellings may be formed. Periosteal reactive phenomena of sunray type are minimal or absent, owing to the cortical bone destruction; but reactive new bone may be laid down beneath the elevated periosteum. Because of the central destruction proceeding outwards, pathological fracture is common.

The existence of this tumour illustrates in excellent fashion the mutability of primitive mesenchyme.

Osteogenic Sarcoma in Paget's Disease.

Paget's disease is probably more common in Australia than in most other countries, and according to some senior radiologists is more common relatively in Sydney than in other parts of this continent. Yet nothing is known of its cause or of the exciting factor which produces a complicating osteogenic sarcoma in a small minority of the patients. It has been suggested that 10% of sufferers ultimately may develop sarcoma; it seems most likely that this figure is at least five times too high.

Osteogenic sarcoma supervenes as a late manifestation of the disease and almost entirely accounts for that moiety of osteogenic sarcoma occurring in the fifty to seventy years age group. It is not known to occur in the fibroid more than the reparative or sclerosing stage of the disease, and most commonly is an osteolytic variety rather than a sclerosing bone-forming tumour. It occurs generally in the shaft of long bones, reversing the usual incidence in juvenile patients, in whom tumours are usually found in juxtaepiphyseal situations. The tumour, being lytic, readily causes pathological fracture and is prone to form massive, disabling and painful tumefactions. Metastasis is rapid and inevitable. In my experience this group of tumours has proved completely resistant to attempts at palliative irradiation, and early amputation is advised to save the patient as much local discomfort as possible, though amputation stump recurrences are only too frequent.

Radiation Osteogenic Sarcoma of Bone.

Osteogenic sarcoma may appear as a late complication of heavy irradiation received by bone. The mechanism of production of the tumour is not understood. Sarcoma may develop in connective tissue damaged by excessive radiation effects, just as carcinoma may develop in over-irradiated skin. The calcium and phosphorus in bone account for the fact that under comparable conditions bone absorbs about two and a half times more energy than does soft tissue from a medium quality deep X-ray therapy beam. Thus it is often difficult to know the real amount of radiation energy absorbed by the bone during radiation treatment, and dose statements are usually underestimates.

Many cases of radiation sarcoma have now been reported; they may follow ingestion of α-ray emitters (for example, radium), and radioactive isotopes like strontium, which become concentrated in the bones, readily produce sarcoma. X radiation has produced its quota of cases, and the minimum dose, estimated as soft-tissue dose required to produce an osteogenic sarcoma, is stated as 3000*r*. It is most unlikely that this dose is ordinarily carcinogenic; most cases have followed much heavier dosage.

Tebbett and Vickery (1952) have reported a case following heavy irradiation of the orbit for retinoblastoma; Spitz and Higinbotham (1951) have reported sarcoma in the spine following irradiation of lumbar glands; and cases have followed irradiation of giant-cell tumours of bone in young people. Jones (1953) recently reviewed the literature and collected in all 39 cases. Sarcoma occurred in 13 cases of irradiated normal bone, in 17 cases of irradiated tubercular joints, and in three cases of giant-cell tumour.

This review of literature and clinical material shows that excessive dosage has been used in practically all cases. Benign giant-cell tumours will respond usually to quite low doses of radiation; if they are not so responding, the diagnosis may be wrong or other treatment should be used. Giant-cell tumours in children are probably better treated surgically on account of risks to epiphyseal growth rates, and not because of the risk of producing osteogenic sarcoma. With dosage in normal ranges the radiotherapist need not fear complications of osteogenic sarcoma.

Osteogenic Sarcoma following Other Rare Causes.

It is necessary for the sake of interest to mention that cases are on record in which osteogenic sarcoma has developed upon *myositis ossificans*, in callus at the site of ununited fractures, in acromegaly and in fibrous dysplasia of bone (Geschicter and Copeland, 1952). I have encountered no cases arising from these causes.

Malignant Giant-Cell Tumour of Bone.

Osteoclastoma must receive mention, especially as it is believed that the osteoblast and osteoclast have common tissue of origin. The benign giant-cell tumour is only too well known.

The malignant variant tends to be atypical in all its manifestations. Radiologically it possesses features which are in part characteristic of a benign giant-cell tumour; but other features raise doubts—for example, the eccentricity of its origin, the irregularity of its trabeculation, and the destruction of cortex—and these features suggest the possibility of osteogenic sarcoma.

Histological examination of the initial section may suggest typical benign giant-cell tumour, curettage of such a malignant variant is likely to lead to speedy recurrence, amputation may be followed by distant metastases or recurrence in the stump, and radiation therapy does not produce the regeneration so typically seen in the benign

tumour. Irradiation does hold the tumour after an initial period of increased bone absorption; the same thing is seen in the benign tumour. The tumour tends to become walled in; but in my treated patients no bone regeneration has occurred within the central tumour mass, as occurs in the benign variety.

The typical histological picture is that of an active spindle-celled stroma in which are cells in mitosis. Giant cells are numerous, and in general are smaller and have but few nuclei compared with the benign tumour. In my experience two types of distant metastases have occurred from such a tumour—those metastases which have reproduced the giant-cell picture exactly, and a group which shows a spindle-cell type of sarcoma only. The spindle-cell stroma is probably the real tumour parenchyma, being derived from the mesenchyme common to osteoblast or osteoclast. Fusion of nuclei to form giant cells represents specialization to form osteoclasts. Therefore an anaplastic tumour would be expected to show spindle cells only, and so metastases without giant cells are easily explained, without the need for regarding the tumour as a variant of of an osteogenic sarcoma.

Reticulum-Cell Sarcoma.

Reticulum-cell sarcoma is regarded as a tumour arising in the reticulo-endothelial tissues of bone marrow, where it does appear as a primary tumour; but bone may be secondarily invaded by reticulum-cell sarcoma starting elsewhere in the reticulo-endothelial system.

The primary cases encountered have been very few, but a somewhat typical appearance is recognized. The tumour appears to commence toward one end of the shaft of a long bone and spreads toward the centre of the bone. Cortex and medulla become completely destroyed, and the bone becomes of uniformly moth-eaten lacy texture. The margins are ragged and irregular and expanded, there is little or no classical periosteal reactive phenomena, and the liability to pathological fracture is great.

However, on review of histological material from one of our cases, in which the tumour radiologically appeared to be a classical juxtaepiphyseal osteogenic sarcoma, a rediagnosis of "reticulum-cell sarcoma" replaced an earlier diagnosis of "cellular osteogenic sarcoma" made in days before the reticulum-cell sarcoma was recognized. Thus no typical radiological picture can be said to exist.

The tumour does seem to be quite reasonably radiosensitive, but the diagnosis can be established only after histological examination. Atypical forms are radiologically quite indistinguishable from osteogenic sarcoma.

Metastases from Osteogenic Sarcoma.

Metastasis occurs early via the blood-stream, for the tendency of tumour cells to line blood sinusoids is well known. Examples are on record of spread by lymphatics—parosteal tumours in particular are credited with such capacity, but I have seen only three examples of metastases to lymph glands. A chondrosarcoma of the body of the mandible produced massive involvement of upper cervical lymph nodes, and in two cases of sarcoma supervening on Paget's disease clinical spread occurred to inguinal and axillary glands respectively. Direct spread up and down bone is always more extensive than radiologically obvious.

The common sites of tumour deposition are the lungs and bone; any other organ is likely. The radiologist sees extraordinary pictures due to metastases in which bone formation has occurred, and on films I have had demonstrated to me secondary deposits in heart and in liver. The formative secondary deposits in bones may produce remarkable pictures.

Some of these secondary sclerosing tumours grow very slowly, and one of my patients came to autopsy with a lung completely replaced by a bony mass weighing six pounds. I have recently seen X-ray films of another patient whose primary growth had been amputated, and whose pulmonary ossific secondary deposits have changed but little during the past four years.

Treatment of Osteogenic Sarcoma.

The first method of treatment considered for a peripheral osteogenic sarcoma is usually amputation; but amputation alone, when practicable, has given very poor results. Detailed results of treatment have been published by many authors (Table I), and it is seen that no result better than 20% five-year survival for amputation alone has been attained. Radiation therapy alone has generally failed to produce any useful result.

In 1936 the late G. F. Stebbins, of Lambeth Hospital, informed me that he had been able to show radiation response in bone sarcoma by using many small doses spread over a prolonged time. In recent years there have been numerous reports (which have been summarized by Cade, 1952) of the use of pre-operative irradiation in the treatment of bone sarcomata. Techniques for the most part use high dosage in a short period of a few weeks, and amputation follows soon after. Irradiation is found to inhibit the activity of the tumour temporarily, some radiological evidence of regression is seen within four to eight weeks, and the delay between diagnosis and amputation to allow irradiation is not thought to be detrimental.

TABLE I.

Representative Results of Treatment of Osteogenic Sarcoma.

Authors.	Results.
Coley and Harrold (1950) ..	59 five-year cures from 252 patients.
Geschicter and Copeland (1949)	26% five-year cures in osteoblastic sarcoma. 7% five-year cures in osteolytic sarcoma.
Tudway (1953)	4 five-year survivals from 33 patients.
Price (1952)	6 five-year survivals from 28 patients, two of whom died later of their disease.
Cade (1952)	13 of 86 patients survived five years.
Bergin (1953)	3 of 20 patients surviving five years.
Platt (1951)	19 of 120 patients survived five years or more. 17 of 85 patients survived five years.
Kaye Scott (present series, 1938–1950)	13 of 32 patients survived five years, four died of their disease later.

Ferguson (1940) showed that early operation saved only 8% of patients, while delayed operation gave 29% of five-year survivals, and he advised that pre-operative irradiation be instituted and immediate operation postponed.

McNattin (1944) described a technique in which massive doses of radiation were used over a period of about a year. His method produced a high proportion of instances of tumour control; but the high dosage used generally involved destruction of the overlying skin, a matter of no very great importance when amputation followed and healthy skin flaps could be obtained.

Since receiving Stebbins's personal advice nearly twenty years ago, I have worked out a policy involving the administration of small doses given intermittently over a period of nine to eighteen months. There is a reasonably sound basis of radiobiological theory favouring such a method of attack, and considerable experimental evidence has come to hand which would appear to justify postponement of immediate operation.

In Melbourne a technique of irradiation has been developed which delivers radiation dosage of the order of 150*r* per session to the tumour, three to four times per week; the initial course is continued for ten weeks with the delivery of a tumour dose of 4500*r* to 6000*r*, with the use of multiple ports, and half-value layer 2·0 to 2·5 millimetres of copper. Care is taken not to produce more than a moderate skin erythema, and dosage is reduced if blistering appears imminent. After the first course of ten weeks a rest period of ten weeks is allowed, and then another course of treatment is started with the object of giving a further tumour dose of 3000*r* in ten weeks. Then a rest of three months is allowed and a third course is given of approximately the same amount, depending on the skin tolerance.

Provided the tumour shows response, treatment is continued, but it is suspended if distant metastases appear. Earlier amputation is undertaken if the tumour is not

showing control by irradiation, there being no evidence of distant metastases.

Prolonged treatment along these lines produces a first-degree skin reaction in four to six weeks, which reaches its height at the seventh week. At this stage treatment often has to be slowed to avoid a vesicating reaction; but this characteristic rhythmic reaction usually subsides, even though treatment is continued. The well-being of the skin must be maintained so that subsequent treatment may be given.

Relief of pain and cessation of tumour growth are noted as immediate effects of the institution of irradiation; but diminution of swelling may not be evident till the six-weeks to eight-weeks stage. The persistence of local pain suggests lack of response to irradiation.

At the twelve-weeks stage the recession of the soft-tissue tumour mass is associated with radiological evidence of repair. Increased deposition of calcium within the tumour and healing by new bone formation in areas previously destroyed are seen, fluffy margins bordering the neoplasm become sharply outlined, and periosteal repair is a dominant feature. During the following twelve months under intermittent treatment, ragged areas of bone destruction become rounded off or filled in as bone repair slowly progresses.

All the radiobiological knowledge which can be gathered about the behaviour of connective tissues under irradiation strengthens the belief that low-dose long-term therapy is a correct method of radiation attack on osteogenic sarcomata.

Scott (1937) showed that connective tissue tumours had relatively low radiation sensitivity when compared with epithelial tumours. He showed that cells in mitosis were more sensitive than resting cells of the same tissue. A dividing cell could be destroyed by a dose one-tenth to one-fifth of that necessary to kill a resting cell. The increased radiosensitivity of cells in mitosis is referred to as mitotic sensitivity. The sensitivity of tumours derived from one or another parent tissue parallels that of the tissue of origin and is referred to as "tissue sensitivity". Thus theoretical and practical experience shows that the specialized sarcomata are not responsive to usual radiation techniques when moderately high doses are given over periods of about four weks, because their tissue sensitivity is low.

Radiation given over such a period in amount sufficient to destroy an osteogenic sarcoma will cause massive death both of the neoplasm and of its stroma—that is, radio-necrosis. In responsive epithelial tumours there occur death and absorption of individual neoplastic cells without death of the stroma—a process called necrobiosis. The attainment of such a result must be the object in radiation therapy of any neoplasm. Radiation attack on the resistant tumour group has to be planned on lines completely different from that used in treating the more sensitive epithelial neoplasms.

Administration of small repeated doses is designed to attack mitotic sensitivity, when low doses will damage that proportion of the cells in division. Therefore, treatment has to be continued over a long time in an effort to catch every cell as it comes into mitosis. We know further that one of the effects of non-lethal radiation on resting cells is to prolong the resting period. So it is logical, first to lengthen the interval between doses after treatment has been in progress for some time, and second, to allow rest intervals between courses of treatment.

McNattin used large doses continued over a long period in an effort to give a high dosage to the tumour, and so took a year to reach his goal; it is believed that it was not the high dose he used that produced the effect, but the time he took over the irradiation. The same result probably would have been produced with lower fractions given in the same overall time, as it is believed that his result was actually attained by damage to cells in mitosis.

Examination of my clinical material shows that approximately three-quarters (21 of 27) of the patients treated with long-term irradiation have shown local response and tumour recession.

At first it was hoped that such a response would indicate local cure. In three of the first group of patients treated by this low-dose long-term method in the late 1930's the tumour recurred locally after four and a half, six and seven years respectively. But one other patient treated at the same time and not subjected to amputation remains well at the present day. It was therefore obvious that prolonged irradiation alone was not generally curative, just as surgery alone had not been able to meet the situation. The next step seemed to be that surgery, as a post-radiational measure, should be combined with the X-ray therapy. At this stage of determination of policy some of the following questions were reconsidered.

Does immediate amputation possibly stimulate the growth and appearance of distant metastases? Can pre-operative irradiation in any way modify the development of distant metastases? Can amputation produce better results if carried out as a delayed proceeding? If blood-borne tumour dissemination is such an early event in the history of osteogenic sarcoma, how can postponement of ablation of the primary tumour influence the outcome?

The experiences with immediate operation over the years suggested that growth of distant secondary deposits might be accelerated as a result of operation. The theory is held that damage to any normal tissue cells liberates growth-promoting substances which stimulate the formation of granulation tissue to allow repair. Massive tissue damage, such as would occur at amputation, may liberate large quantities of such substances, which would stimulate growth of distantly deposited tumour cells. Such a theory could explain many an instance of rapid growth of secondary deposits after surgical procedures.

Growth-promoting substances, called trephones by Carrel, are elaborated by leucocytes and lymphocytes, and Fischer regards these substances as specific growth hormones with the special function of stimulating mitosis. Growth-promoting properties of protein breakdown products have been extensively studied, and large peptides in particular have been found to exert a stimulating action on mitosis (Hughes, 1952).

Dissemination of tumour cells from a primary osteogenic sarcoma is known to occur early, and it must be assumed that every patient when first examined has blood-borne metastases, even if these cannot be detected by clinical or radiological means.

The body has a defence mechanism against deposited malignant cells (Willis, 1934), and it seems likely that only a fraction of deposited neoplastic cells ever survive to become obvious secondary nodules. The destruction or temporary walling off of secondary tumour deposits in the lungs is well described by Willis. These body defence mechanisms must, if possible, be assisted, and the ill effects of immediate operation on microscopic tumour emboli must be prevented.

The preliminary irradiation above described has been shown to inactivate the tumour locally in a high proportion of the cases. It then seemed reasonable to suppose that in responsive tumours the flooding of tumour emboli into the blood-stream would be stopped relatively early. The patient would have an increased chance of overcoming already deposited cells if the onslaught on the pulmonary capillary bed could be stopped. The defence is assisted by general measures designed to maintain nutrition and well-being, attention being paid to hæmoglobin levels, diet, vitamins and tonics, while rest to the tumour-bearing part by immobilization may assist in diminishing dissemination.

Therefore, operative procedures should be postponed until such time as the lungs have had a reasonable chance of overcoming any preexisting microscopic deposits, provided that radiation control of the primary tumour is being attained. My case records show that a high percentage of metastases appear within three months and a much smaller proportion between three and nine months; but if a patient survives for twelve months the risks of development of pulmonary metastases are greatly diminished.

It was therefore decided that a patient showing a satisfactory preliminary response to irradiation should wait at

least twelve months, preferably eighteen, to see that pulmonary metastases do not appear. If indications were then favourable, amputation should be undertaken. The selection of this time is arbitrary in part, but is based upon the time of appearance of secondary deposits in treated patients and the knowledge that the likelihood of permanent cure from irradiation is remote.

If amputation is refused or impossible on account of site, further prolonged courses of irradiation are administered at longer intervals. Every effort must be made to preserve the skin from late necrosis due to excessive radiation.

As must be anticipated, many patients treated have shown a response to irradiation, but have developed pulmonary secondary deposits before the conclusion of the initial course of irradiation; one cannot imagine that immediate amputation could have saved this group. Treatment is suspended in such cases unless irradiation is indicated to prevent such complications as later fungation.

No clinician can contemplate with equanimity the results of surgery alone, and the foregoing scheme has been developed in an attempt to follow logical principles of radiobiology and pathology. If the principles are right, then results should be improved. But it must be remembered that the patient's chance of survival depends solely on his own capacity to destroy the blood-spread tumour emboli liberated before the irradiation inactivated the primary tumour. If in the following eighteen months this destruction of secondary deposits does in fact occur, then subsequent operation can be undertaken without the risk that growth-promoting substances liberated by inevitable damage to normal tissues will cause stimulation of these metastases.

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APPENDIX.

Osteogenic Sarcoma: Statistics from the Radiotherapy Department, Royal Melbourne Hospital, 1938-1950.

There were 27 cases of osteogenic sarcoma treated at the Royal Melbourne Hospital radiotherapy department from 1938 till 1950; 15 patients were males, 12 females. (Five cases of sarcoma on Paget's disease are analysed separately; the grand total is thus 32.)

The patients' ages were as follows: under ten years, two; under twenty years, 11; under thirty years, two; under forty years, four; over forty years, eight.

The sites of the tumours were as follows: tibia, four cases; fibula, one case; femur, 10 cases; humerus, four cases; pelvis, four cases; maxilla, one case; ribs, two cases; radius, one case.

Histological proof of the type of tumour was obtained in 17 of the 27 cases. There was only one five-year survival in cases in which histological proof was not obtained. There were 13 survivals for five years or more in cases in which histological proof was obtained.

The diagnoses were as follows: osteogenic sarcoma, 19 cases; chondrosarcoma, seven cases; reticulum-cell sarcoma, one case.

The results of treatment are as follows: Of five patients who received one course of X-ray therapy, all developed secondary deposits. Of 11 patients who received two courses, eight are dead, one had a local recurrence at four and three-quarter years and is alive with the disease at five and a half years, and two are alive and well after more than five years. Of 12 patients who were given three or more courses of X-ray treatment, the figures for survival are as follows: (i) 11 survived for five years or more, two of whom had a recurrence at four and a half years, one at five and a half years, one at six years and one at eight and a half years; (ii) one patient survived for three years, having refused elective amputation. Of 13 patients who survived for five years or more, eight are believed cured, four subsequently died of the disease, and one is alive with the disease.

The effect of primary irradiation was as follows: local control by irradiation was obtained in 21 cases; in only six cases was the tumour non-sensitive.

The figures relating to radiation therapy and elective amputation are as follows: Five patients with osteogenic sarcoma underwent elective post-irradiational amputation; one developed secondary deposits at four and a half years and died at five and a half years; four are alive and well

six, eight, ten and thirteen years afterwards respectively; all these tumours were histologically proven. Two patients suffering from chondrosarcomata underwent post-irradiational amputation; one survived for five and a half years and one for twelve years, and both died from cardiac causes without evidence of recurrence; both tumours were histologically proven.

Late operation produced the following results: Three patients underwent amputation after late recurrences of the primary growth at three, four and a half and five years respectively; one died at four years, one survived for five years and died of the disease, and one is alive and well after sixteen years; all the tumours were histologically proven.

The figures relating to cases in which no operation was performed are as follows: There were five patients in the group; one (pelvis affected) had a local recurrence at four and three-quarter years and is alive at five and a half years with the disease; one (pelvis affected) developed a local recurrence at six years and died at eight years; one (rib affected) developed a local recurrence at eight and a half years and is presumed dead; one (femur affected) is alive and well after sixteen years. (In this case only, of 14 in which the patients are still living, histological proof was not obtained.)

Sarcoma on Paget's Disease.

Five patients with untreated osteogenic sarcoma supervening on Paget's disease were examined in the clinic in the period under review; four were males and one was a female. Their ages were as follows: over forty years, one; over sixty years, three; over seventy years, one. The sites of the tumours were as follows: humerus, two cases; ilium, two cases; tibia, one case.

Three patients received one or two short courses of X-ray therapy without improvement; one received one course (ten weeks) of X-ray therapy without improvement; one, unsuitable for X-ray therapy, was referred for amputation.

Four of the patients survived for five to seven months, and one survived for sixteen months. In two cases clinical involvement of regional lymph glands was evident before the patient's death.

Conclusion.

When these five cases of sarcoma on Paget's disease are added to the main group of 27 cases, the survival figures are as follows: five-year survivals, 13 out of 32 patients; believed cured, eight out of 32 patients.

INNOCENT SYSTOLIC MURMURS IN CHILDHOOD.[1]

By DOUGLAS STUCKEY,
From the Royal Alexandra Hospital for Children, Sydney.

AN innocent mumur may be defined, in accordance with Levine (1937), as one which occurs in the absence of any disease or important abnormality, and which therefore has in itself no clinical significance either at the present time or in the future. A distinction must be made from a functional murmur, which occurs in the absence of organic disease of the valves of the heart, but often in association with heart disease or other disease processes; for example, the murmurs of functional mitral or tricuspid incompetence, the mid-diastolic murmurs associated with patent *ductus arteriosus* or with ventricular septal defect, or the pulmonary systolic murmurs in patients with anæmia or thyrotoxicosis.

Of 400 patients examined at the Congenital Heart Disease Clinic in recent years, 60 were considered to have a normal heart with an innocent systolic murmur. Of the whole group, the results of post-mortem examination were available in 19, in 57 the diagnosis was confirmed at operation, and in 89 either angiocardiography or cardiac catheterization had been carried out. This study is based on the 60 patients with an innocent systolic murmur. A hæmoglobin estimation, an electrocardiographic examination and a radiological examination were carried out in all cases, in addition to careful clinical examination. Many of the children were examined on several occasions at intervals of twelve months.

The ages of the patients at first examination ranged from one to ten years. In infants aged under twelve months, respiratory sounds and tachycardia made auscultation difficult. A murmur heard under these conditions was, in our experience, likely to be a significant one, but a final decision was often deferred until the child was older. Thirty-nine of the children were males and 21 females, a male preponderance of almost 2:1. A similar male preponderance in children with innocent murmurs was found by Shapiro (1939).

In 17 instances the mother had suffered from rubella during the early months of pregnancy, and in one each from varicella and ordinary measles. The high incidence of maternal rubella occurred because a large group of affected children was specially referred for examination on account of the possibility of congenital heart disease. Four children had suffered from a febrile illness shortly before the murmur was discovered, but it is very doubtful whether this was of any significance.

The Murmurs.

Characteristically the murmurs were mid-systolic, of short duration occupying less than half of systole, and of only slight or moderate intensity (Shapiro, 1939). Following Levine (1937), we have graded the intensity of murmurs, using four grades corresponding to the descriptive terms soft or slight, moderate, loud, and very loud; these were roughly equivalent to grades II to V of Levine. In 50 of the children the murmur was recorded as grade I, in 10 as grade II, and in none was the murmur louder than grade II. In eight patients the murmur was described as musical or squeaky, and in the remainder as blowing. In two patients the murmur was loudest at the mitral area, in the remainder in the left parasternal line; 31 murmurs were best heard in the second, or the second and third intercostal spaces, 22 in the third or third and fourth intercostal spaces, and five in the fourth intercostal space. Some of these murmurs could be heard at the mitral and aortic areas as well, but wide propagation was unusual.

Physical Examination.

In general, apart from the murmur, physical examination gave findings within normal limits. In particular, the radial and femoral pulses were normal, there was no evidence of hypertrophy of either ventricle on palpation, there were no thrills, and in the pulmonary area the second heart sound split normally during inspiration and the pulmonary component was of normal intensity. In the normal child with a thin chest wall, slight right ventricular pulsations may be felt to the left of the sternum, and occasionally pulmonary valve closure may be felt in the second left intercostal space. Both these physical signs are usually considered abnormal in adults.

There were abnormalities of the chest wall in four patients. One had a depressed sternum and three had asymmetry of the chest, which was flattened on the left side in two patients and bulging on the left side in the third. The systolic blood pressure was 120 millimetres of mercury or more in six patients, the highest reading being 145 millimetres of mercury.

Special Investigations.

The hæmoglobin value was within normal limits in all cases. Radiological examination showed that the heart was of normal size and that the vascular markings in the lungs were within normal limits in all cases. In 13 patients the main trunk of the pulmonary artery appeared to be enlarged, in two of them considerably. In two patients a right aortic arch was present.

The electrocardiogram was within normal limits in all cases, showing no evidence of hypertrophy of either ventricle. An *RSR* complex in lead V1 or V2 was noted in seven patients. This pattern occurs normally in perhaps 20% of infants, and is found less frequently with increasing age, being uncommon in normal subjects aged twelve years or more.

[1] The substance of a paper presented at a meeting of the Australasian Cardiac Society on May 9, 1955.

Mechanism.

The surprising thing is not that innocent murmurs occasionally occur, but that murmurs are heard so seldom in the normal heart. This must be regarded as evidence of the hæmodynamic efficiency of the heart as a pump, so that the blood circulates with varying velocities through heart chambers and valve orifices of different sizes without setting up sufficient turbulence to produce an audible murmur.

In the present series of sixty patients, abnormalities of the chest wall were found in four, slight hypertension in six, a right aortic arch in two, and a large pulmonary artery in 13. Chisholm (1937) suggested as a possible mechanism that when there is dilatation of the pulmonary artery involving the pulmonary valve ring, during systole the normal valve cusps are too short to relax completely against the walls of the pulmonary artery, and form a triangular orifice smaller than the dilated vessel beyond. A rather similar effect in normal aortic valves has been beautifully demonstrated by McMillan (1955). Blood flow through a normal valve ring into a dilated artery beyond could thus produce eddying and turbulence, and so an audible murmur.

Many of these murmurs were strictly mid-systolic in timing, and heard almost as well at the mitral and aortic areas as at the left sternal border, which suggests that they were aortic in origin. Slight dilatation of the ascending aorta beyond a normal aortic valve orifice may be the mechanism in these cases, as in the so-called "murmur of aortic sclerosis" in older persons with hypertension, associated with dilatation and unfolding of the aorta.

The high incidence of innocent murmurs in children whose mothers have a history of rubella during pregnancy is of interest. Apart from congenital heart defects, cataracts and deafness, these children show many slight variations from normal bodily architecture, such as very little subcutaneous fat, abnormalities of the teeth, and the typical elfin facies (Dods, 1951). Perhaps slight variations in the form of the heart or great vessels short of a recognizable congenital defect also occur.

In general, it is suggested that most innocent parasternal systolic murmurs are produced by variations in the shape or calibre of the great vessels distal to a normal pulmonary or aortic valve.

Discussion.

The clinical importance of innocent systolic murmurs in childhood lies in the recognition of their innocent nature, and in the distinction from murmurs due to rheumatic or congenital heart disease. The innocent murmur is usually loudest in the left parasternal line, and is mid-systolic, of short duration and of no more than moderate intensity. Supporting evidence is provided by a normal second sound, no evidence of ventricular hypertrophy either clinically or in the electrocardiogram, and normal radiological appearances, except perhaps prominence of the main trunk of the pulmonary artery.

The systolic murmur of rheumatic carditis, while variable in intensity, usually fills systole and is best heard at, or lateral to, the mitral area. With ventricular septal defect, the murmur fills systole (Leatham, 1952) and is loud and almost always accompanied by a thrill. The characteristic continuous anastomotic murmur of patent *ductus arteriosus* should not be confused. With atrial septal defect, the second sound is usually widely split. In all these conditions, mid-diastolic murmurs, evidence of ventricular hypertrophy either clinically or in the electrocardiogram, and radiological appearances of cardiac enlargement or of pulmonary plethora will often confirm the diagnosis. The distinction of innocent systolic murmurs from those found in aortic or pulmonary stenosis may be much more difficult. In both these conditions the murmur is usually loud and accompanied by a thrill. With mild pulmonary stenosis the pulmonary component of the second sound is characteristically diminished and delayed (Leatham, 1952), and there is usually some slight evidence of right ventricular hypertrophy, either clinical or electrocardiographic. In mild aortic stenosis the murmur is louder than grade II, and a definite thrill should be felt over the large arteries in the neck, even if it is not present on the chest wall.

The diagnosis of an innocent murmur is often made by exclusion—that is, the presence of a murmur in the absence of any recognizable organic lesion. It should be possible from the site, character and intensity of the murmur to make a more positive diagnosis of innocent murmur, and even to suggest whether it is aortic or pulmonary in origin.

Should the parents be told that a murmur of this type has been heard in the child? We think that they should, it being stressed at the same time that the heart is entirely normal and that the murmur is slight and of no significance. This information will often prevent diagnostic confusion when the child is subsequently examined by some other doctor. Recognition of the innocent nature of a murmur may avoid an erroneous diagnosis of rheumatic carditis in the presence of vague ill-health or of some other febrile illness, and will often prevent unnecessary restrictions being placed upon normal, healthy children.

Summary.

Of 60 children considered to have an innocent systolic murmur, four had minor abnormalities of the chest wall, six slight hypertension and two a right aortic arch, and in 13 prominence of the main pulmonary artery was found on radiological examination.

It is suggested that most innocent parasternal systolic murmurs are produced by variations in the shape or calibre of the great vessels distal to a normal pulmonary or aortic valve. The importance is stressed of distinguishing these innocent murmurs from those due to rheumatic or congenital heart disease.

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THE FIRST LUMBAR ROOT SYNDROME.

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A COMMON painful condition exists which has not previously been described as an entire syndrome; because it is frequently mistaken for other common conditions, mainly lower abdominal, a description of it is here published in the hope of preventing some of these errors.

I have recognized this condition for a number of years in its various guises, and a large series of cases of what is here described as the first lumbar root syndrome has been collected in this time. In view of the fact that it is mistaken for many of the common painful lower abdominal conditions, it is surprising that it has missed a place in the literature; but I am sure that those who have had difficult cases of lower abdominal pain will recognize in this condition the solution to many of them. It has few of the characteristics of the intercostal neuralgias publicized some years back, but nevertheless it is part of them.

In differential diagnosis this condition is no respecter of the fields of medicine, as it is seen in all of them, particu-

larly by those specialists covering this region of the body—surgeon, gynæcologist, urologist and orthopædist—who will at times be puzzled and perhaps at fault unless the condition is considered in a diagnosis.

Basically this condition is a painful one occurring over part or whole of the first lumbar segment unilaterally or bilaterally, with definite areas of usually well localized tenderness, which is without doubt of skeletal and not of visceral origin. It is one of the commonest of all segmental pains, and has many things in common with the other great root lesion, sciatica.

Anatomical Factors.

Segmental pain occurs most frequently in relation to those vertebræ in which the greatest strain occurs—that is, where there is an alteration in the curve of the spine, and/or at the junction of the fixed and mobile segments. The function of the fifth lumbar vertebra and the sacrum is well recognized as being in this category, particularly if the transverse processes of the fifth lumbar vertebra are set high so that the combined ilio-lumbar ligaments attached to them no longer exert their sling-like action and restrain mobility. An analogy may be drawn where the first lumbar vertebra set in similar circumstances is fixed by the lateral arcuate ligaments to a well-developed twelfth rib. If the first lumbar vertebra is well stabilized by these ligaments, then the junction of the first and second lumbar vertebræ will be the less stable segment—that is, the junction of the mobile lumbar segments with the more fixed thoracic group. When the twelfth rib is small, or when the first lumbar transverse process is represented by an articulated rib, the first lumbar vertebra will not be stabilized and the junction of the twelfth dorsal and first lumbar vertebræ may be the more unstable.

The vertebral bodies and the intervening disk spaces in the upright position are primarily concerned with weight-bearing. The apophyseal joints carry out the function of check ligaments, and as such are subjected to much of the strain taken by the vertebræ in carrying out this function. In the upright position, in this part of the spine these joints do not bear weight, except perhaps the fifth lumbar vertebra. When the body is flexed it is the apophyseal joints, not the disks, that become weight-bearing in addition to their normal check function. These apophyseal joints represent a see-saw with the body and disk as the fulcrum, so that movement of one will be mirror-imaged by the other, and as a corollary strain of one in certain positions may strain the other.

The anterior and posterior spinal nerve roots converge in the foramen, becoming a single root as they emerge from it. Here the posterior root lies on the capsule of the apophyseal joint, and so is likely to be involved in any pathological condition which occurs in it, particularly as the roots fit fairly snugly in the foramen. The posterior root is protected from the back of the vertebra and disk by the anterior root itself, so that lesions involving the posterior sensory root are more likely to occur in this situation—apophyseal lesions rather than vertebral or disk upsets; the anterior root will bear the brunt of the pathological change in these structures.

The apophyseal joints, being similar to limb joints and having their own capsule, synovia and articular cartilage, are liable to damage in the same way as limb joints like the ankle. The reaction to injury will be traumatic inflammation with increased synovial fluid, thickened inflamed synovia and capsule and pannus of the articular cartilage. Any nerve lying in proximity to an inflammatory lesion is liable to irritation, partly from the inflammation, and also because inflammation lowers the threshold of pain in a nerve. The posterior root as it lies on the capsule of the apophyseal joint is likely to be affected by traumatic inflammatory changes involving these joints resultant on injury, whether a single trauma, repeated minor traumata or the result of persistent strain. The last-mentioned is of importance; most clinicians have seen the painful, œdematous, hot foot resulting from acute foot strain, and these apophyseal joints are not unlike the mid-tarsal joints in this respect.

The single nerve root, after leaving the foramen, shortly gives off its posterior primary ramus, which passes backwards lateral to the superior articular process and the intertransverse muscle, there dividing into two branches, medial and lateral; the medial branches are (i) muscular to the corresponding deep muscles of the back, and (ii) sensory to the spinous processes and laminæ. The lateral branches are chiefly cutaneous, and in the case of the upper lumbar group are directed obliquely downwards and laterally among the fibres of the sacro-spinalis, becoming superficial by piercing the lumbo-dorsal fascia. The anterior primary ramus of the first lumbar nerve, after receiving the sympathetic grey *rami communicantes*, enters the abdomen under the medial arcuate ligament to cross in front of the *quadratus lumborum*. The ilio-inguinal and ilio-hypogastric nerves may arise as separate nerves from the trunk, but generally diverge under cover of the iliac crest. These nerves eventually become superficial by piercing the three great muscles of the abdominal wall, in turn running between them for a varying distance. The important clinical fact is that the ilio-inguinal nerve pierces the aponeurotic external oblique just above the external abdominal ring with some constancy, one branch continuing with the cord to the testicle, and another branch passing to the inner side of the thigh.

The ilio-hypogastric at a higher level pierces the internal oblique in the upper part of the iliac fossa, sometimes above umbilical level, and again pierces the external oblique in the medial part of the iliac fossa. The ilio-hypogastric is responsible for the lateral cutaneous branch of the first lumbar segment which crosses the iliac crest, extending to trochanter level.

It has been found that most of the so-called trigger points in relation to pain in various parts of the body always correspond to the anatomical site of a nerve perforating some fascial structure, whether it be joint ligament, tendinous insertion or fascial expansion.

Normally the perforations by these nerves with their covering of areolar tissue are neither tender nor painful, and when these nerves or their trunks become irritable these sites may become exquisitely tender and the site of severe pain on any movement or contraction of the structure through which they pass, although the intervening nerve passing in the muscle layers may not even be tender to pressure.

So it is with the first lumbar syndrome to be described. The sites of maximum pain and tenderness are at the edge of the *erector spinæ* opposite the centre of the twelfth rib, and in front in the iliac fossa near the edge of the *rectus abdominis* close to McBurney's point or more medially in the case of the ilio-hypogastric, and in the lower part of the iliac fossa in the case of the ilio-inguinal. These sites of pain and tenderness correspond to those of many of the common visceral complaints, as will be further demonstrated.

Origin of Segmental Pain.

Pains of segmental distribution fall into the following three common ætiological groups: firstly, from irritation of the nerve root itself; secondly, from irritation of the segmental fibres in a nerve or its branches; thirdly, from pain referred from a structure supplied by these fibres.

In the case of the first lumbar segment, the first of these may result from first or second lumbar disk prolapse or other intraspinal lesions (in this series these cases were few or unproven), or from involvement of the posterior root in the neighbouring disease arising in the apophyseal joint, generally inflammatory from trauma. In the second group the pain may arise from any condition irritating the nerve along its course. In the third group—pain referred from a structure with a first lumbar segment supply—again the apophyseal joint is suspect.

In the first of these categories, in which a disk lesion is the aggravating factor, one would expect the anterior root to be involved more frequently; but one has often seen large nucleus prolapses of the lumbo-sacral disk of which pain is the predominant feature, with little motor change except some spinal muscle spasm and perhaps loss of muscle tone or ankle jerk. It is presumed from this that

minimal pressure will produce pain; but far greater compression is required to produce motor loss. Motor loss corresponding to the first lumbar segment is difficult to determine, as the cremasteric reflex arc may be altered on the sensory side, and loss of muscle tone or power of the lower part of the abdomen owing to segmental overlap is difficult to determine, but may show as a bulge on coughing or standing, similar to the Mulgain's bulge seen in many normal subjects, usually of spare build. Only in a few cases has radiographic examination revealed evidence of disk collapse, and in a few others in which this has been sought by exploration adequate evidence has been lacking, though too few patients have been examined in this way.

Irritation of the nerve along its course giving rise to the radiation of pain over the first lumbar segment has been seen on several occasions from trauma in the region of the external ring, direct trauma giving rise to local hæmatoma, and indirect trauma from muscle damage; one of these patients subsequently developed an inguinal hernia.

Suggested Ætiology.

The most feasible ætiological factor seems to me to be likely to arise from upset in the apophyseal joint, either root irritation subsequent on traumatic arthritis, or as a referred pain over its corresponding segmental supply, in the same way as a painful hip will radiate pain over the corresponding obturator segments to the inner side of the knee. This is undoubtedly the case in the many examples arising in vertebræ already the site of osteoarthritis which has developed from previous damage, the pain being now set going by some minor trauma, insufficient to upset a normal joint. This is common to all joints affected by osteoarthritis.

Many will have noted the complaint of pain of typical first lumbar segment distribution radiating in the lower part of the abdomen, in association with sciatica or lumbosacral backache. It has also been noted that a primary first lumbar root syndrome has subsequently been followed by sciatica or low backache. The common denominator in both these conditions is muscle spasm and associated scoliosis. It is probable that whatever the initiating factor in the muscle spasms, whether it be first lumbar or fifth lumbar, the apophyseal joints are subjected to strain at these, the more unstable sites in the lumbar part of the spine, and that the secondary phenomena have developed on the primary initiating factor. This is further suggested by the fact that a low epidural block to cover the first sacral segment and relieve the muscle spasm will generally automatically relieve the secondary first lumbar root symptoms. Similarly, when the first lumbar root is the initiating irritator, the first lumbar block will relieve the lumbosacral symptoms. In fact, the initiated muscle spasm is responsible for much of the aching pain associated with both these lesions.

Clinical Phenomena.

The first lumbar syndrome has many things in common with the group of sciaticas, but in itself is a separate entity, and the great importance of its recognition is the frequency of its confusion with a kaleidoscope of common conditions seen by all practitioners. Consequently it is a general surgical problem, not one narrowed to any particular specialty. It is this common confusion, resulting often in economic and sometimes tragic loss from ignorance of its existence, that prompts the publication of these data. In a review of 100 cases over the past few years, I find that most patients have had what would otherwise be unnecessary investigations, operations, hospitalization and economic loss.

In considering the condition as a separate entity it is most important to realize that the pain, which is its predominant feature, may be over the whole segment—that is, loin pain and backache corresponding to the posterior primary ramus, lower abdominal pain, which may be up to the level of the umbilicus, and sometimes over the iliac crest to the upper lateral aspect of the thigh (the ilio-hypogastric element), as well as pain extending down to the testicle and inner aspect of the thigh (the ilio-inguinal element). In a small percentages of cases, pain such as this, over the full coverage of the first lumbar segment, was complained of; but just as it is often bilateral, one side being predominant in the history, so frequently does the complaint of pain cover only part of the whole. Thus there may be pain only in the loin, or pain in the testicle, or in the upper part of the iliac fossa. This distribution is analogous to that of the first sacral segment in sciatica, in which the pain may be over the whole segment from buttocks to toes, or in the buttock only, the calf only, or the toes only.

So it is with the tender areas; they may be in the loin, in the external ring region and the upper part of the iliac fossa, or in any combination of sites, unilateral or bilateral, although as a rule the tender spots are more constant to the three sites than is the pain pattern.

The onset may be spontaneous, but often follows an injury, industrial or otherwise, received in the flexed position. It is interesting to note here that when the body is bent the apophyseal joints are weight-bearing—the only time when they are; also, that in this position the posterior annulus is on the stretch. The traumatic type of pain generally occurs in patients whose tissues are becoming less elastic—the thirty-five to forty years age group—as an occupational hazard in a man who still thinks he can manage at this age what he could do in the garden at the age of twenty years. In the industrial field, it is generally the skilled tradesman or foreman class who suffer from lifting. Here the invariable diagnosis is a torn muscle (a condition which in itself is extremely uncommon).

As often as not, the onset is gradual, and the frequency with which the condition occurs in women with this gradual onset suggests that here at least acute trauma is not the exciting factor. However, women do more work in the half-bent position than men.

The pain pattern may be of three types—mechanical, inflammatory, or a combination of the two.

In the mechanical sequence, the pain is aggravated by general or particular movements or positions. In the acute stage almost any movement is painful; there is muscle spasm with scoliosis concave to the side of the lesion, and this spasm is to some extent responsible for the generalized aching pain. Special movement may result in pain, as may contraction of the abdominal muscles, in which case the hyperæsthetic nerves are compressed as they penetrate the muscle layers. This is not a constant feature except in the acute cases. One position which seems to be fairly universally unpleasant is lying on the affected side, and most patients cannot go to sleep unless they lie on the opposite side or back. Once they are at rest, sleep is not interfered with unless the sufferer rolls over. Generally in the mechanical sequence the pain is relieved by morning, becoming worse with movement during the day.

In this series the mechanical is by far the most common sequence; but it may be necessary to inquire directly about its relationship to motion and position.

In the inflammatory sequence typically the pain is severe at night, with morning stiffness which decreases with daily movement.

The combined sequence, mechanical and inflammatory, is that usually seen in the arthritic patient. Here the pain has a mechanical sequence in relation to movement and position; at the same time, as the result of the day's mechanical irritation, there is a superadded inflammatory sequence covering the night and morning.

In all inflammatory lesions there is a throbbing element added to the pain, which is of two types, typical of nerve root lesions as a whole. Firstly there is a constant unpleasant ache, with intermittent sharp, shooting exacerbations. The pain may be burning; but seldom is there any paræsthesia or hyperæsthesia suggesting that the primary abnormality is not one of compression of the root. Evidence of diminished function in the nerve has been met with on only a few occasions.

Now that the distribution of pain in this syndrome, the type of pain, and the possible tenderness which may occur in a number of combinations have been considered, it is

easy to see how confusion with visceral lesions may readily occur; in this series a large number of patients have been referred after all common diagnoses and investigations have been considered.

Differential Diagnosis.

One of the common errors will be a diagnosis of renal colic, and many of these people have already been investigated by pyelography and urine examination. This is a natural error, when pain radiates from the loin down the iliac fossa to the testicle, with tenderness in the renal angle corresponding to the perforation of the posterior branch, and also in the iliac fossa. This diagnosis is often supported in the minds of many if, on inquiry into the urinary history, pain on micturition is admitted. Acceptance of such correlation is far too ready, as few patients with renal colic have pain on micturition unless cystitis also exists. It is pointed out here that many patients with the first lumbar root syndrome complain of pain on micturition, which on careful observation is shown to be due to painful contraction of the abdominal musculature either in initiating or in completing the act.

Probably the most important differential point in separating these two conditions is in the history, from which a mechanical or inflammatory sequence can be discovered as well as the frequent bilateral nature of the pain in the first lumbar root syndrome. A colic is often referred to as a sharp pain; but it differs from the lancinating pain of a root lesion by doubling the patient up, rising to a *crescendo* of intensity, whereas the pain of a root lesion is sudden, sharp and stabbing, and all movement is brought to a standstill until it has passed off. It is important to remember in the inquiry that some of these patients are in the age group in which arthritic changes and urinary symptoms are coexistent, or in which in younger women a difficult labour has left a residuum of frequency and urgency of micturition from a damaged anterior vaginal wall.

When the pain is bilateral, in women particularly, that diagnosis of pyelitis which seems to be used to cover any difficult pain in this region is made—the more so if the amateur pathologist has the urinary crystals slightly out of focus in the microscope so that the rings look like pus cells. Here pain and tenderness in both loins aid iliac fossæ make the diagnosis seem assured. But the patient is apyrexial, and a mechanical sequence is not that of pyelitis. Further, in the genito-urinary field pain radiating into the testicle, which may become excessively hyperæsthetic, has been mistaken for acute epididymitis, and on one occasion torsion—this latter solely on the severity of the pain. Once the patient can be coaxed into allowing examination of the organ, it will be found not to vary from the normal site except for the acute discomfort.

When the pain and tenderness in the main are localized to the right iliac fossa, sometimes with radiation to umbilical level (ilio-hypogastric), and when in addition there is muscle guarding of this segment, what more is required for a diagnosis of appendicitis? Seldom if ever in this condition are there associated visceral symptoms, unless the pain is so severe as to nauseate the patient; in addition, in any patient who has lost sleep and has continuous pain, anorexia may be present.

It is probably in appendicitis that the greatest number of errors are committed. It is easy to confuse the two conditions, and appendicitis is a common condition which all can deal with, while appendicectomy is one of the early operative lessons of many surgeons. Poynton (1950), from examination of sections of removed appendices, has shown a large number to be histologically normal; this may be from misinterpretation of the physical signs, particularly the pain and tenderness. This latter finding is further substantiated in the clinical histories of persons with the syndrome here described, in which the pain was still present, of a similar type to that suffered prior to the acquisition of an appendicectomy scar.

A similar pain on the left side may be confused with diverticulitis. There are a few clinical conditions which produce pain and tenderness in the left lower quadrant of the abdomen, diverticulitis being one of the more common conditions called to mind; but this is not nearly so common as pain from this first lumbar root syndrome—diverticulosis maybe, but not diverticulitis. It is mentioned here that muscle spasm involving the lower abdominal segment has the "feel" of an indefinite abdominal mass extending obliquely down the iliac fossa, and will be tender apart from the common tender sites found in this condition.

Several patients have been submitted for operation for inguinal hernia when sudden pain and tenderness in the region of the external ring have developed, usually the result of a strain or lift at work. Both these lesions may develop from the same cause, and as such both are compensatable; as a rule the inguinal hernia is the easier to cure. The ilio-inguinal pain may develop subsequently, being referred from a lesion in the back or from local damage at the site of the external ring.

Apart from appendicitis and renal colic, the largest group in the differentiation of this syndrome comes from the gynæcological field, and most women with this complaint pass into this specialist field at one time or another.

Most can remember the classical text-book picture of pain and tenderness relating to tubo-ovarian disease as represented diagrammatically by symmetrical hatched circles about an inch above and lateral to the pubic spines. Pain and tenderness here or in the iliac fossa, unilateral or bilateral, perhaps with pain over the hips (the lateral branch of the ilio-hypogastric) in combination with backache, menstrual or otherwise, paint a fairly vivid text-book picture of pelvic disorders. If in addition bimanual pelvic examination is painful, particularly if the abdominal hand is the heavier of the two, this may confirm the suspicion that the patient is tender in the fornix on vaginal examination. If exploratory laparotomy reveals to the casual operator, ignorant of gynæcological pathology, a follicular cyst, this completes the diagnosis. Should the pain recur after ten days' rest in bed or make itself felt on the other side, the age-old panacea of adhesions is a diagnosis which in fact may be truthful enough if a subsequent intestinal obstruction develops. The orthopædist sees this condition as backache, strained abdominal muscles or hip-joint pain. The first two mistakes are made usually if the pain follows a lifting strain, when a patient develops acutely painful and tender areas either in the lumbo-costal angle or in the lower part of the abdomen, possibly associated with pain on contraction of the muscles concerned.

A number of patients referred on account of hip-joint pain have been encountered with pain in the groin and the inner aspect of the thigh (ilio-inguinal branch) and over the lateral aspect of the hip (ilio-hypogastric lateral branch), aggravated by active flexion, forced external rotation and passive extension, which involve the abdominal muscles as well as the hip joint. The hip joint may be flexed to relax the abdominal muscles, and so the patient will limp.

An attempt has been made to present this condition as vividly as possible; but the presentation cannot be vivid enough when one considers the economic loss and disability that result from an error of diagnosis in so many of these conditions confused with this, a common but generally unrecognized syndrome, when a careful, painstaking history is all that is required.

Many of the conditions confused with this syndrome have already been enumerated, as they are the common ones; but into this picture comes any condition producing backache or pains in the side. The essential basis of diagnosis is the recognition of this condition as a syndrome; once it is recognized, its differentiation from other conditions is relatively easy, particularly when the pain sequence—generally mechanical or mechanical inflammatory—is obtained in the history. Careful elucidation of the pain type and sequence generally separates this from visceral pains, as does the absence of associated visceral symptoms.

As the ætiology is as yet incompletely understood, treatment is somewhat empirical; however, it does seem that the apophyseal joints may well be the origin of the pain, either directly or indirectly, and in the few patients subjected to operation these joints have shown the abnor-

mality of early arthritic changes. Like many of the irritative sciaticas, the commonly invoked prolapsed nucleus is not to be found.

Treatment.

Treatment has been based on two things. First, since the pain is generally mechanical in sequence, mechanical means can be employed to relieve it. External fixation in the form of a spinal brace to immobilize the joint should be satisfactory, but has been seldom used, mainly because women, who are among the common group of sufferers, refuse to wear such cumbersome apparatus for any length of time. A few patients with long-standing pain who have received only temporary relief by other means have been subjected to operation, disk exploration and subsequent fusion. The exploration has been investigational only and is now not carried out.

The most satisfactory method of fusion has been by the fixation of a number 2 curved plate to the spines of the twelfth dorsal and first and second lumbar vertebræ, and subsequently the insertion of a cancellous bone graft; at the same time partial apophysectomy is carried out to aid fusion of these joints. The alternative method is screw fixation of the twelfth dorsal and first lumbar and the first and second lumbar apophyseal joints, but this is more difficult on account of the sagittal direction of these joints. To obtain the correct angle the drill and screw are inserted through the spinous process or interspinous ligament; this makes for easier technique.

The fact that but few patients have required radical treatment says something for the success of the conservative measures, which with few exceptions consisted of lumbar root block with a local anæsthetic agent. This, in addition to its therapeutic value, provides considerable diagnostic assistance. Experience with other root and other somatic pains, particularly those of irritative rather than compressive origin, has shown the value of local anæsthesia as means of relief. The theories relating to this will not be discussed here; but the fact that the temporary relief provided by a local anæsthetic agent can become a permanent cure obviously invokes a reversible process, whether from release of muscle spasm or from the reversal of a chemical process such as has been suggested in the branched axon theory of Sinclair *et alii* (1948).

First lumbar root block is easily performed as an outpatient procedure, provided that no excess of local anæsthetic agent is injected which will diffuse to other lumbar nerves, so affecting the quadriceps supply.

The first lumbar transverse process is located two fingers' breadth away from the spinous process, which itself is roughly opposite the centre of the twelfth rib. After intradermal injection the needle is advanced to the transverse process, then angled to pass below it a further one-half to three-quarters of an inch where the nerve is situated. One interesting feature of this syndrome is that penetration of the deep fascia (lumbo-dorsal) by the needle is painful (hyperæsthetic), and this may produce a referred pain to the anterior or lateral distribution of the first lumbar segment as well as to its posterior distribution. This phenomenon fits with the theory of branched axons of Sinclair *et alii*. When the needle is advanced to the region of the nerve root, either the needle itself or more particularly the increasing pressure of the injected local anæsthetic agent will reproduce the pain. If this reproduction of the pain complained of can be accomplished, the diagnosis is not in doubt, and relief can be expected.

On most occasions a single injection satisfactorily placed has given permanent relief from this pain. Other patients have had repeated injections, each time with temporary relief, recurrence taking place after periods of time varying from a few days to a few months. A very small percentage had no relief other than the period of action of the local anæsthetic agent. It is possible that in these a persistent mechanical lesion such as a displaced nucleus had been overlooked.

The greatest importance of the introduction of this condition as a syndrome in itself is to press its recognition on to those who have not yet realized that it is frequently confused with other common conditions met with by all classes of practitioners, who, failing to realize its presence, are apt to embark on operations and investigation, for some of which they will be called to account by the patients themselves when the pain still remains.

The fact that such a large number of cases in this category have been encountered over the last few years since it has been recognized as a syndrome makes its statistical frequency in my series as great as that of sciatica from all causes. In all cases referred from another practitioner it passed unrecognized, solely owing to lack of knowledge of its existence. Almost without exception the pain was thought to be of visceral origin, sometimes categorically, sometimes half-heartedly for want of a better explanation. It is only by directing attention to the condition that it can be brought into the differential diagnosis of those ignorant of its features. Once it is recognized, its acceptance is beyond doubt, and it will be found to explain many of those odd pains in the right or left iliac fossa which for so long have been an anathema to the practitioner, as they do not quite fit in with the common visceral conditions.

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"DIAMOX" IN THE MANAGEMENT OF GLAUCOMA.

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THE essential feature of glaucoma is a raised intraocular pressure, as was first established in 1830 by William MacKenzie, a Scottish physician. Cases in which the cause of this raised intraocular pressure is known are grouped as secondary glaucoma, and the essential treatment is that of the underlying abnormality. When the cause is not known, these cases are classified as primary glaucoma, and treatment is directed towards lowering the intraocular pressure to normal limits. This may be achieved by the use of meiotic drugs administered as eye drops, or by surgical methods which aim at (*a*) assisting in the drainage of aqueous humour from the eye or (*b*) the destruction of part of the ciliary body with a consequent decrease in the amount of aqueous humour formed, the functionally inadequate drainage mechanism being thereby enabled to cope with the smaller volumes of aqueous humour formed.

A new method of treatment, embodying a new principle, has been found in the use of "Diamox" (acetazoleamide) in the management of glaucoma. The purpose of this paper is to report the use of "Diamox" in twenty cases of glaucoma and to discuss its role in the management of this disease.

"Diamox" is a heterocyclic sulphonamide introduced as an orally effective diuretic, its mode of action being to act as an inhibitor of carbonic anhydrase in the kidney. The theoretical basis for the use of this agent in glaucoma stems from the concept of bicarbonate secretion in the formation of aqueous humour by the ciliary body (Friedenwald, 1949). Carbonic anhydrase has been demonstrated in the ciliary body and iris of the rabbit by Wistrand (1951), and it has been postulated that "Diamox" inhibits this carbonic anhydrase; experimental evidence to confirm this inhibitory action has been recently put forward by Green, Capper, Bocher and Leopold (1954). As a result of carbonic anhydrase inhibition by "Diamox", bicarbonate enters the aqueous at a reduced concentration; the aqueous sodium concentration is likewise lowered, and there then follows a fall in osmotic pressure, which results in less water influx and a lowering of intraocular pressure (Breinin and Gortz, 1954). Clinical evidence to support this mode of action has been provided by tonographic

studies in cases of glaucoma, in which it has been demonstrated that the fall in intraocular pressure after "Diamox" is not associated with any improvement in the drainage mechanism of the eye (Becker, 1954*b*; Grant and Trotter, 1954). Additional evidence is provided by cases of glaucoma with complete closure of the angle of the anterior chamber, in which "Diamox" may produce a considerable lowering of pressure (Grant and Trotter, 1954).

TABLE I.

Types of Glaucoma Studied.

Type of Glaucoma.	Number of Cases.
Primary:	
Acute congestive	7
Chronic congestive	1
Chronic simple	4
Secondary:	
Associated with iridic neovascularization	3
Associated with anterior uveitis	2
Associated with aphakia	1
Glaucoma capsulare	1
Associated with dislocated lens	1

Clinical trials with "Diamox" were first reported by Becker (1954*a*), who recorded outstanding pressure-lowering effects; more recent reports have followed (Grant and Trotter, 1954; Posner, 1954; Breinin and Gortz, 1954). Since Becker's paper was published "Diamox" has been used in a variety of cases of glaucoma, and my experiences will be recorded in this paper.

TABLE II.

Fall in Intraocular Pressure which can be Fairly Attributed to "Diamox" in Each Case of Glaucoma Studied.

Type of Glaucoma.	Case Number.	Condition of Eye or Intraocular Pressure. (Millimetres of Mercury, Schiötz.) Before "Diamox".	After "Diamox".
Primary:			
Acute congestive	*I*	*40*	*26*
	II	55	38
	III	48	22
	IV	70	17
	V	50	0
	VI right eye	41	23
	VI left eye	30	18
	VII right eye	21	25
	VII left eye	47	36
Chronic congestive	VIII	30	19
Chronic simple	IX	(See *Figure III*)	—
	X	(See Figure IV)	—
	XI right eye	29	25
	XI left eye	29	25
	XII	40	25
Secondary:			
Iridic neovascularization	XIII right eye	75	45
	XIII left eye	45	22
	XIV	+++ (Steamy cornea)	+ (Clear cornea)
	XV	100	64
Anterior uveitis	XVI	66	30 (Soft)
	XVII	65	
Aphakia	XVIII	— (Steamy cornea)	20 (Clear cornea)
Glaucoma capsulo-cuticulare	XIX right eye	44	15
	XIX left eye	35	20
Dislocated lens	XX	65	63

Material.

The cases studied are indicated in Table I. Most of these patients were admitted to hospital, appropriate local treatment was given, and later "Diamox" was administered. The same routine was followed with four patients who were treated in their own homes and remained ambulatory. The usual dose of "Diamox" given was 500 milligrammes *statim*, the same dose being repeated in twelve hours, and this was followed with 250 milligrammes twelve-hourly. When there were clinical indications this dosage scheme was modified or curtailed.

Results.

A summary of the fall in ocular tension which can be fairly attributed to "Diamox" in each case is presented in Table II.

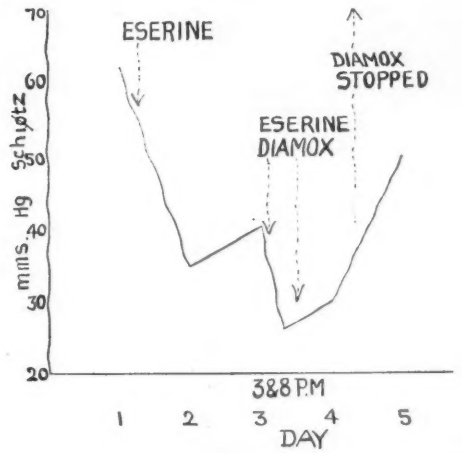

FIGURE I.

Case I. Acute congestive glaucoma. With cessation of "Diamox" the tension commenced to rise again.

Acute Congestive Glaucoma.

The results in acute congestive glaucoma are clear-cut and dramatic, the fall in tension being greater the higher the initial level. In Case I (Figure I) the tension was controlled with eserine drops and "Diamox"; but cessation of the latter (due to lack of supplies) resulted in a rise in tension necessitating surgical interference. In Case III (see Figure II) a similar rise in ocular tension followed cessation of "Diamox", but with repeated exhibition of the drug the tension was controlled and the eye prepared for surgery under more favourable circumstances. The effect of "Diamox" in lowering the pressure in a normal eye is seen in Case VI, in which the tension in the left eye is at the upper limit of normality (see Table III).

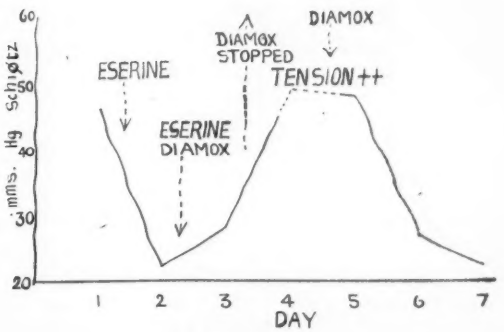

FIGURE II.

Case III. Acute congestive glaucoma. The tension-lowering properties of "Diamox" are demonstrated here on two separate occasions.

Chronic Congestive Glaucoma.

One case of chronic congestive glaucoma was studied; the patient remained ambulatory throughout the treatment. In 1952 he underwent a right corneo-scleral trephining operation, and the tension in the left eye was kept steady with eserine and pilocarpine drops. In spite of this, the tension in this eye started to rise, and "Diamox" was used to control this (see Table IV). He was the only patient in this series to show side effects due to "Diamox" (nausea and tingling in the fingers), and these were eliminated by a slight reduction in dosage.

TABLE III.

Case VI: Acute Congestive Glaucoma.

Date.	Treatment.	Intraocular Pressure. (Millimetres of Mercury, Schiötz.)[1]	
		Right Eye.	Left Eye.
31.12.54	Eserine	48	20
3. 1.55	Eserine	40	33
4. 1.55[1]	Eserine *plus* "Diamox" ..	41	30
5. 1.55	Eserine *plus* "Diamox" ..	23	18

[1] Intraocular pressure measured before commencement of "Diamox" therapy.

TABLE IV.

Case VIII: Chronic Congestive Glaucoma.

Date.	Treatment.	Intraocular Pressure Left Eye. (Millimetres of Mercury, Schiötz.)
29.11.54	Eserine, pilocarpine	30
20.12.54	Eserine, pilocarpine	30
21.12.54	Eserine, pilocarpine, "Diamox" ..	30
23.12.54[1]	Eserine, pilocarpine, "Diamox" ..	19
30.12.54	Eserine, pilocarpine, "Diamox". ("Diamox" dose reduced.)	16
5. 1.55	Eserine, pilocarpine, "Diamox". ("Diamox" dose reduced.)	17
14. 1.55	Eserine, pilocarpine, "Diamox". ("Diamox" dose reduced.)	17

[1] Slight nausea with tingling in fingers.

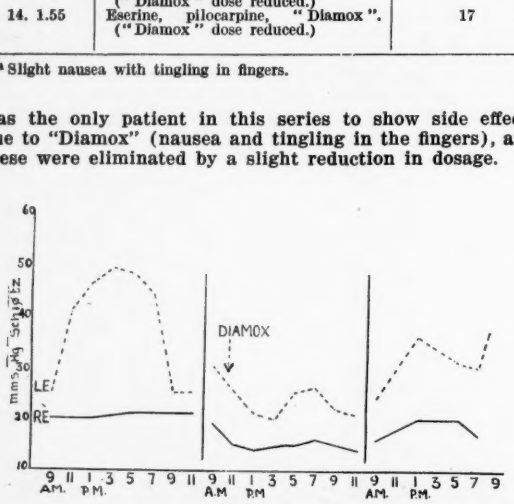

FIGURE III.

Case IX. Chronic simple glaucoma: phasic variation of tension. "Diamox" lowers the tension of both the glaucomatous and the "normal" eye.

Chronic Simple Glaucoma.

Four cases of chronic simple glaucoma were studied; in two of these (Cases IX and X) (see Figures III and IV) the diurnal phasic variation in tension was recorded. In Case IX (see Figure III) the effect of "Diamox" can be more clearly demonstrated; but in Case X other factors, such as bed rest, have confused the result. The extreme importance of allowing for these factors in assessing the effects of "Diamox" in chronic simple glaucoma is well shown by studying these two cases.

Glaucoma Associated with Iridic Neovascularization.

There were three cases of glaucoma associated with iridic neovascularization—two of thrombotic glaucoma and one of glaucoma in a "diabetic eye" (retinopathy with new vessel formation on the iris). The patient in Case XIII was examined in October, 1954, when she had occlusion of the right central retinal vein, and in January, 1955, when she had acute glaucoma in the same eye (see Table II). The fall in tension in the left eye must be due to "Diamox", and part of the fall in the right eye must be due to this drug also; the patient concurrently had intensive eserine therapy to the right eye.

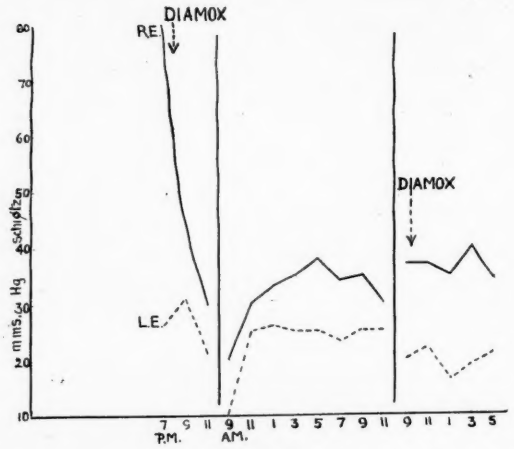

FIGURE IV.

Case X. Chronic simple glaucoma: phasic variation of tension.

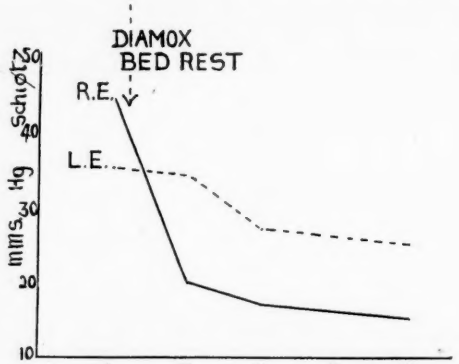

FIGURE V.

Case XIX. *Glaucoma capsulo-cuticulare.* Both bed rest and "Diamox" contribute to the fall in ocular tension.

The patient in Case XIV (thrombotic glaucoma) was not submitted to Schiötz tonometry in his state of acute glaucoma; but after the exhibition of eserine drops with "Diamox" there was a considerable subjective improvement with relief of pain, clearing of the œdematous cornea and lowering of the ocular tension as estimated digitally.

Case XV was that of a diabetic, who was admitted to hospital with acute glaucoma, the tension in the left eye being 100 millimetres of mercury (Schiötz). Intensive eserine therapy together with "Diamox" caused a fall of tension to 64 millimetres of mercury (Schiötz) on the following day.

Glaucoma Associated with Anterior Uveitis.

In the two cases of glaucoma associated with anterior uveitis, "Diamox" contributed to the lowering of tension in this form of secondary glaucoma.

Aphakic Glaucoma.

One patient suffering from aphakic glaucoma was treated and a good response obtained with "Diamox".

Glaucoma Capsulo-Cuticulare.

One patient (Case XIX) suffering from *glaucoma capsulo-cuticulare* demonstrates the beneficial effect that bed rest may have on raised ocular tension (see Figure V). At the time when bed rest was commenced "Diamox" was administered, so it is probably incorrect to attribute the fall in pressure solely to either of these agents.

Glaucoma Associated with Dislocated Lens.

"Diamox" had no beneficial effect in the one case of glaucoma associated with dislocated lens, and cyclodiathermy was carried out to lower the raised tension.

Comment.

The introduction of "Diamox" has provided a new approach to the glaucoma problem, and it is now possible to lower the intraocular pressure in a dramatic fashion in almost all glaucomatous eyes. Thus in twenty cases there has been only one in which no demonstrable fall in pressure resulted.

In normal eyes the demonstrable effect due to "Diamox" is not great (left eye of patient in Case VI, Table II), and this is in agreement with the findings of other workers (Becker, 1954*a*; Breinin and Gortz, 1954).

The outstanding results have been obtained with the acute forms of glaucoma, both primary and secondary (see Table II). In the management of acute glaucoma, local therapy must be continued together with "Diamox". In this way, in acute (primary) congestive glaucoma a two-fold attack is made (*a*) on the drainage mechanism of the eye, with meiotics, and (*b*) on the site of aqeuous humour formation, with "Diamox". An acute crisis can thus be overcome, the intraocular pressure lowered, and the eye whitened and prepared for operation, which can be undertaken at a subsequent time when it will be safer for the patient and easier for the surgeon. Synergism of "Diamox" with meiotics is discussed by Breinin and Gortz (1954), and they quote two of their cases illustrating this; but I have not clearly observed any such synergistic action.

In general the management of secondary glaucoma is greatly helped by "Diamox", but the underlying disease must, of course, be treated at the same time. Both Grant and Trotter (1954) and Breinin and Gortz (1954) have found it useful in glaucoma associated with anterior uveitis, and my experience has been similar. Thrombotic glaucoma, always presenting a great problem in management, is assisted by "Diamox"; our two cases clearly show this (Table II).

In chronic glaucoma several considerations must be borne in mind in assessing the value of a new therapeutic agent. The first of these is the phasic diurnal variation in intraocular pressure. To date only Breinin and Gortz (1954) have considered this aspect in evaluating "Diamox", and we have "phased" some of our cases. The phasic variation of ocular tension over twenty-four hours must be considered in chronic glaucoma, and not just one isolated daily tonometric reading. (This same statement applies to meiotic therapy. One wonders in how many cases of chronic glaucoma, supposedly controlled by meiotics, the intraocular pressure rises above the upper limit of normality at some time during the twenty-four hours.) The second consideration is bed rest. The phasic diurnal variation curve varies according to whether the patient is in bed or up and about carrying out his normal daily affairs. Case X (Figure IV) and Case XIX (Figure V) illustrate this difficulty. The third consideration is the influence of other therapy, such as meiotic drops.

In our studies to date the influence of these factors has become apparent, and sometimes makes the assessment of the value of "Diamox" in a particular case difficult. In future observations allowance must be made for these factors in the evaluation of "Diamox", especially in the possible long-term treatment of chronic glaucoma.

Dosage.

The routine used has been mentioned above, and from the literature to date there appears to be some latitude in dosage. Larger doses are used than in the treatment of cardio-renal œdema. Whereas Grant and Trotter (1954) state that "Diamox" should be given to the extent that the patient can tolerate its side effects, Breinin and Gortz (1954) state that the aim should be to administer the smallest dose which will control the ocular tension.

As the aim of glaucoma treatment is to produce a normal intraocular pressure over the twenty-four hour period, it appears that "Diamox" should be given at such intervals as to eliminate the peaks in the diurnal intraocular pressure curve. The appropriate times of administration can be calculated from the knowledge that the maximum fall in pressure after an oral dose of 500 milligrammes of "Diamox" occurs approximately three hours later (Becker, 1954*a*; Breinin and Gortz, 1954).

"Diamox" may be given parenterally as well as orally, and this should be helpful with some cases of acute glaucoma associated with vomiting. Thus in Case XIII the patient would have been helped considerably by the parenteral administration of "Diamox", as she was nauseated and vomiting, partly owing to the glaucoma, and partly owing to a coincidental attack of Ménière's disease.

Toxicity.

Paræsthesiæ, anorexia, nausea, drowsiness and skin rash have been recorded as following "Diamox" therapy (Breinin and Gortz, 1954; Grant and Trotter, 1954). Only one of our patients (Case VIII) had paræsthesiæ, and in general it does not appear that these manifestations of toxicity are frequent. Hepatic cirrhosis and acidosis are contraindications to "Diamox" therapy.

Summary.

1. The use of "Diamox", a potent inhibitor of carbonic anhydrase in the ciliary body and iris, has been studied in the management of glaucoma.

2. Its greatest use is in the treatment of the acute rises in tension in acute glaucoma. In these cases it need be used only for a short time, so that the tension may be lowered, the eye whitened, and operation performed under favourable conditions. This appears to be the main use of "Diamox" established to date.

3. In chronic glaucoma the use of "Diamox' 'is more difficult to judge; certain factors which must be considered in assessing any new agent for the treatment of glaucoma are stressed, and further studies on the use of "Diamox" in chronic glaucoma are indicated.

4. Amongst the secondary forms of glaucoma "Diamox" has been found particularly helpful in the management of that form associated with anterior uveitis and in thrombotic glaucoma.

5. "Diamox" provides adjuvant therapy in glaucoma; meiotics for primary glaucoma or the appropriate local treatment for secondary glaucoma must be simultaneously given.

Acknowledgements.

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Dr. Arthur Joyce, of Melbourne, permitted me to study Cases VIII, XI and XII. Mr. G. W. N. Cunningham, of D.H.A. (Victoria), Proprietary, Limited, distributors for Lederle Laboratories, kindly made supplies of "Diamox" available to me.

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POST-MORTEM FINDINGS IN STILLBIRTH AND NEONATAL DEATH: AN AUTOPSY INVESTIGATION.

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IN a previous paper (Snow and Pearson, 1951) the purpose and method of a special investigation into stillbirths, neonatal deaths and premature births in Western Australia was described, and the preliminary findings based on 457 consecutive cases (including 250 submitted to autopsy) were reported.

The investigation began on August 1, 1949, and was terminated on December 31, 1953, when 1067 stillbirths and neonatal deaths had been recorded. Of these subjects, 742 (including the 250 previously reported) were submitted to post-mortem examination, and the findings are reported in the present paper.

Causes of Death.

Of the 742 deaths, 544 were stillbirths and 198 neonatal deaths. Since it was compulsory to notify stillbirths, this represents the total that had occurred in the Perth district during the survey period. Neonatal deaths were not notifiable, but many practitioners sent these babies for examination to find the cause of death; and almost all had died within the first forty-eight hours of life.

In Table I the causes of death are recorded, together with an additional 325 stillbirths and neonatal deaths which occurred in Western Australia during this period; on these subjects no autopsy was performed.

TABLE II.
Causes of Asphyxia Neonatorum.

Cause.	Number of Cases.
Premature separation of placenta and placental disease	90
Inhalation of meconium	53
Inhalation of *vernix caseosa*	2
Inhalation of mucus	3
Hyaline membrane	2
Ante-partum hæmorrhage	31
Atelectasis	30
Hyoscine-morphine analgesia	4
Alveolar hæmorrhage	3
Prolonged, difficult labour and Cæsarean section	21
Cerebral œdema	7
Cord complications:	
Prolapse of cord	4
Cord around neck	10
True knot	4
Not classified	29
Total	293

Expressed in percentages of the total number of fœtuses on which an autopsy was performed, the causes of death were as follows: asphyxia, 39·7%; injury, 18·0%; malformation, 9·1%; prematurity, 3·9%; toxæmia, 1·7%; Rh incompatibility, 8·6%; other causes, 5·0%; undetermined, 14·0%; total, 100%.

Asphyxia Neonatorum.

Asphyxia neonatorum accounted for the largest number of deaths—293 (39·7%)—and a more detailed list of causes is given in Table II.

TABLE I.
Stillbirths, Neonatal Deaths, and Premature Births in Western Australia (1949 to 1953).

Presumptive Cause of Death.	Autopsy Carried Out.						A Total.	No Autopsy Carried Out.						B Total.	Total A+B.
	Stillbirths.			Neonatal Deaths.				Stillbirths.			Neonatal Deaths.				
	Premature Infants.	Mature Infants.	Total.	Premature Infants.	Mature Infants.	Total.		Premature Infants.	Mature Infants.	Total.	Premature Infants.	Mature Infants.	Total.		
Asphyxia	67	167	234	27	32	59	293	21	59	80	5	—	5	85	378
Injury	12	91	103	9	21	30	133	—	12	12	2	1	3	15	148
Malformation	22	22	44	8	16	24	68	9	11	20	—	1	1	21	89
Premature	8	—	8	21	—	21	29	6	—	6	16	—	16	22	51
Toxæmia	6	7	13	—	—	—	13	17	13	30	3	—	3	33	46
Rh incompatibility	12	29	41	3	20	23	64	2	5	7	—	1	1	8	72
Others	3	8	11	7	19	26	37	1	2	3	3	2	5	8	45
Undetermined	38	52	90	6	9	15	105	29	86	115	15	3	18	133	238
Total	168	376	544	81	117	198	742	85	188	273	44	8	52	325	1067
Grand total			544			198	742			273			52	325	1067

In asphyxia, autopsy reveals general venous congestion, with dark fluid blood in the veins. Petechial hæmorrhages are common on the surface of the heart, lungs and thymus glands. In premature separation of the placenta these petechial hæmorrhages are large and extensive in distribution. Frequently the white matter of the brain is light purple in colour. More extensive hæmorrhage can occur especially in the medulla of the suprarenal glands, sometimes into the abdominal cavity, the cranial cavity and the lungs. Atelectasis and pulmonary congestion are common.

No distinction could be made at autopsy between *asphyxia livida* and *asphyxia pallida*, since the infant was usually cyanotic. This distinction is probably unnecessary.

TABLE III.
Types of Injury.

Injury.	Number of Cases.
Tentorial tear	84 (63·2%)
Falx tear	10 (7·5%)
Ventricular hæmorrhage	10 (7·5%)
Subarachnoid hæmorrhage	7 (5·3%)
Subdural hæmorrhage	7 (5·3%)
Tear of great cerebral vein	9 (6·8%)
Miscellaneous:	
Fracture of skull	1
"Cerebral hæmorrhage"	3
Pulmonary hæmorrhage	1
Tear of pial vein	1
	6 (4·5%)

Inhalation of meconium (52 cases) was diagnosed only when meconium could be squeezed out of the small bronchi in a section of the lung and on the additional sign of meconium in the stomach, beside the usual signs of asphyxia.

Only two cases of hyaline membrane were recognized, but the special staining methods necessary for the recognition of this condition were not used until very late in the series, and other cases were probably missed.

Four deaths were directly attributed to the use of twilight sleep (hyoscine and morphine), two being due to the acute mania produced by this method in the mother. In other cases of asphyxia the use of these drugs was suspected but not proven.

TABLE IV.
Autopsy: Injury (133 Subjects).

Obstetric Factors.[1]	Number of Cases.
Breech delivery	37
Occipito-posterior presentation	16
Forceps delivery	41
Large baby (eight pounds)	33

[1] In some instances more than one of the foregoing factors was associated with the same case.

Artificial Respiration.—Frequently the lungs showed a remarkable appearance resembling acute emphysema with large surface bullæ, and at times surgical emphysema in the mediastinum. A characteristic of these lungs was the way they floated on the top of water, like a "bluebottle" on the sea. Normally the lung of a newborn child which has breathed floats like an iceberg, with little of the lung showing above the water level, or if only a small degree of expansion has occurred, the lung will sink. After seeing these various reactions to the hydrostatic test, which is commonly used in forensic work to determine whether a child has lived, I am quite convinced that the test is almost completely unreliable. This emphysematous lung was always traced back, sometimes with difficulty, to the use of the old methods of artificial respiration, especially mouth-to-mouth breathing and the use of the oxygen catheter in the nose. Not uncommonly in these cases the stomach was found to be distended with air, whereas the normal stomach contains clear mucus. It appeared obvious after inspection of these lungs that too much force had been used, and it was difficult to conceive how the force of the operator's breath could be satisfactorily controlled. Examination of microscopic sections revealed gross destruction of most of the alveoli, and gave the appearance that once this condition had been produced it would have been impossible for the baby to survive.

If when less force is used only partial destruction of alveoli occurs, one wonders whether the infant survives, only to be affected in later childhood by chest complaints such as bronchiectasis and bronchitis. I believe that there might be a field for further investigation of this matter.

In 14 infants whose death was attributed to asphyxia, free blood was found in the abdominal cavity. Of these, seven had subcapsular hæmorrhage of the liver and one a tear of the liver. Most of the hæmorrhages were associated with attempts at artificial respiration by either pressure on the chest or Byrd's method. It would appear that these methods of artificial respiration are not advisable.

Injury.

Birth injury accounted for 133 deaths (18%), and the types of injury are shown in Table III.

In Table IV the presentation, the use of forceps and size of the baby are given.

Tentorial tear was found much more frequently than any other injury (84—63·2%).

Frequently several types of injury occurred.

TABLE V.
Autopsy: Malformation (68 Subjects).

Malformation.	Number of Subjects.
Malformed heart	16 (23·5%)
Anencephalus	15 (22·1%)
Hydrocephalus	9 (13·2%)
Genito-urinary malformation	7 (10·3%)
Malformed lungs	5 (7·4%)
Diaphragmatic hernia	4 (5·9%)
Malformation of alimentary canal	4 (5·9%)
Gross exomphalos	2 (2·9%)
Miscellaneous	6 (8·8%)

Malformation.

Malformation was the cause of death in 68 (9·1%) and is shown in Table V.

Malformed heart occurred most frequently, followed closely by anencephalus.

Genito-urinary malformations were interesting and consisted of congenital absence of kidneys and ureters (two cases), polycystic kidneys (three), rudimentary cystic kidneys (one), Wilms's tumour (one).

As far as can be ascertained from the literature, a Wilms's tumour (metanephroblastoma) is a very rare finding in a stillborn fœtus. According to Potter, no cases occurred in her series, and "in his search of the literature, Wells found only five tumours which he thought undoubtedly existed at birth". The tumour found was a large mass the size of a tennis-ball growing from the anterior surface of the left kidney. The cut surface was hard, compact and white. Microscopic examination of sections verified the diagnosis.

Horseshoe kidney was recorded three times in fœtuses whose death was attributed to malformation of the heart.

Diaphragmatic hernia was the cause of death in four cases, but was found on eight other occasions in lesser degree.

One case of a mermaid occurred.

Rhabdomyoma with tuberosclerosis occurred in one infant.

Congenital malformations were found in nine other infants whose death was attributed to other causes. This made the number of malformed infants 77, or 10·4% of the total.

Rh Incompatibility.

The number of deaths due to Rh incompatibility was high, and this is attributed to several features. At the beginning of this survey a laboratory was established at King Edward Memorial Hospital for the especial purpose of aiding the diagnosis and treatment of Rhesus incompatibility. This meant that many mothers from districts other than Perth came to the hospital for their confinements. The other feature was the routine blood testing for antibodies.

Deaths were divided into the following three main subtypes: *hydrops fœtalis*, 32; *erythroblastosis neonatorum*, 30; anæmia of the newborn, two; total, 64. In all these fatal cases antibodies were found in the maternal blood.

The chief autopsy findings in the subjects of *hydrops fœtalis* were as follows: (i) generalized œdema, especially of the face; (ii) enlarged liver and spleen; (iii) large, pale, spongy, thick placenta with broken surface; (iv) lipoid infiltration of the adrenal cortex, as shown by the bright yellow inner layer of the cortex; this is present even in a grossly macerated fœtus.

Almost all these babies were stillborn, or at least survived for only a short time.

In the fully developed case of *erythroblastosis neonatorum*, diagnosis was easy, and the typical findings were as follows: (i) jaundice of the skin and internal organs; (ii) enlarged liver and spleen; (iii) lipoid deposits in the adrenal cortex; (iv) pial vessels appearing to float like red tubes on a sea of yellow jelly on the surface of the brain; (v) kernicterus; bright yellow staining of basal ganglia; present only in advanced cases; (vi) showed many blood-forming centres containing nucleated red cells found on microscopic examination of sections of the liver, spleen and placenta; (vii) thick, spongy and pale placenta; (viii) antibodies present.

Prematurity.

A diagnosis of death due to prematurity alone was made only when the fœtus was small and not fully developed and no other cause of death could be found. In the category death due to birth injury, 10 deaths due to ventricular hæmorrhage are recorded; these were all deaths of premature infants. Ventricular hæmorrhage is a common cause of death in the premature child.

Toxæmia.

Only 13 deaths were attributed to toxæmia, and only when definite toxæmia was present in the mother and led directly to the fœtal death.

Other Causes.

In the category "other causes" all the neonatal infections are placed; the chief causes of death were as follows: pneumonia, 25; interlobar pulmonary hæmorrhage, three; pneumococcal meningitis, one; glomerulo-nephritis, three; syphilis, one; fibroid degeneration of the placenta, one; craniotomy *et cetera*, three; total, 37.

Undetermined.

There were in the category "undetermined" 105 deaths; 89 fœtuses were macerated, and it was totally impossible to come to any conclusion as to the cause of death. The remaining 16 showed no macroscopic or microscopic abnormalities which could lead to a diagnosis.

Summary.

1. A series of 742 consecutive autopsies was performed on infants stillborn or dead in the neonatal period in Western Australia during the years from 1949 to 1953, inclusive.

2. This was made possible by the introduction of special legislation authorizing the compulsory submission to autopsy of all stillborn infants in the Perth district.

3. The causes of death are tabulated.

4. Some aspects of the causes of death are discussed.

Acknowledgements.

I am indebted to Dr. L. Henzell, Commissioner of Public Health in Western Australia, for permission to publish this paper; to Dr. D. J. Snow, of the Public Health Department, who tabulated all the reports; to Dr. T. Lubbe, who examined all the microscopic sections at Royal Perth Hospital; and to Dr. C. E. Cook, of the Commonwealth Health Department, who initiated this survey.

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LARYNGEAL SWABS FOR THE DETECTION OF TUBERCLE BACILLI IN PATIENTS WITHOUT SPUTUM.

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IN the investigation of patients with radiological opacities when tuberculosis is suspected, it often happens that the patients are unable to provide a specimen of sputum for examination. In such cases the accepted method is to examine the fasting gastric contents, and over the years many workers have shown this to be a valuable and reliable procedure.

More recently the technique of laryngeal swabbing has gained increasing favour in various centres on account of its convenience.

Investigations of the sensitivity of the method have given differing results. Armstrong (1951), in a large series, found one laryngeal swab culture to be as sensitive as one gastric culture, and three swab cultures to be nearly twice as sensitive. Hounslow and Usher (1948) found, in comparison with gastric culture, individual swab culture to be less sensitive, two swab cultures to be approximately the same, and three swab cultures to be better. Forbes *et alii* (1948) found that two swabs gave slightly fewer positive results than one gastric lavage, while Duggan and Delamater (1950) concluded that two or preferably three swab cultures were as accurate as a single gastric lavage. Lundar (1950) and Gilge (1951), after their controlled series of investigations, recommended that laryngeal swabs could advantageously replace gastric lavage. However, Chaves *et alii* (1953) in a large series have reported less favourable results, finding two swab cultures to be approximately 72% as effective as a single gastric culture. This latter investigation included special conditions which required posting of specimens from a large number of clinics with changing personnel. A reasonable interpretation of these varying results would appear to be that the technique employed is a very important factor. That this is so is shown by Mankiewicz (1953), who by a change of method was able to demonstrate a convincing superiority of laryngeal swabs over gastric lavage, as compared with her previous results, in which the advantages, though present, were not so great. Work along the lines indicated by Mankiewicz is now in progress.

We have accepted the overseas results as indicating that three laryngeal swabs give at least as many positive cultures as, and possibly more than, one gastric lavage. Many of the investigators (Hounslow and Usher, 1948, and Armstrong, 1951), when establishing the value of multiple swabs, repeated the swab culture on successive days rather than on the same day. This has obvious disadvantages to both patient and laboratory.

In this investigation we have taken all three swabs on the same day and attempted to determine whether this is inferior to taking the swabs on successive days. In

addition, an estimate has been made of the optimum number of swabs beyond which only an insignificant number of additional positive results are obtained.

Material and Methods.

The laryngeal swabs were secured from out-patients without sputum who attended the chest clinic either for the diagnosis of a pulmonary condition or for observation and treatment of pulmonary tuberculosis. During the investigations 578 swabs in triplicate were taken from 454 patients, some of whom were examined on more than one occasion.

Technique.

A nursing sister took the majority of swabs, the following method being used.

Sterile cotton wool swabs on aluminium wire milled at one end were sterilized and stored in test tubes until wanted for use. On being withdrawn from the tube, the wire was bent against the wall to form approximately a right angle. The swab was then moistened in sterile water, the patient's tongue held down by a depressor, and the swab passed down towards the larynx. The patient usually coughed at this stage, otherwise he was instructed to do so. As has been pointed out by Armstrong (1951), the swab seldom enters the larynx.

The process was repeated twice more, and the laryngeal swabs were then placed in numbered tubes of 2·5% oxalic acid solution and sent to the laboratory. After fifteen to twenty minutes the swabs were sown directly on to Löwenstein-Jensen's medium without neutralization, two tubes being used for each swab.

Results.

Percentage of Swabs Yielding Cultures of Tubercle Bacilli.

Of 578 swabs in triplicate, a positive culture was obtained from one or more on 66 occasions—that is, 11·4% of the examinations gave positive results. In comparison, 456 routine sputum cultures from the clinic patients produced 79 (17·3%) positives.

Incidence of Positive Cultures from Each Swab.

The number of positive cultures grown from each of the three swabs was approximately the same, as may be seen from the following tabulation:

Positive cultures from all three swabs—32.	
Positive cultures from two swabs:	
First and second	7
First and third	6
Second and third	2
Positive culture from one swab only:	
First	8
Second	5
Third	6
Positive cultures from first swab	53
Positive cultures from second swab	46
Positive cultures from third swab	46
Positive results if only one swab taken	53 (80·3%)
Positive results if only two swabs taken	60 (90·9%)
Positive results from all three swabs	66 (100%)

The foregoing tabulation shows the value of taking three swabs, and the relatively uniform distribution of positive findings between the first, second and third swabs. This indicates that the material producing a positive culture is not exhausted when the three swabs are taken at one session. To test this further, a comparison has been made with the results obtained when swabs were taken on successive days (Armstrong, 1951). The first swab yielded 120 positive cultures, the second swab 123, and the third swab 121. There is no significant difference between the two results ($\chi^2 = 0{\cdot}60, n = 2, P > 0{\cdot}70$).

Optimum Number of Swabs.

The first swab alone produced 53 positive results (80·3%), the first and second swabs together produced 60 positive results (90·9%), the third swab added a further six positive results (9·1%).

The results were set out graphically and the curve was extended to obtain an estimate of the number of additional positive results to be expected from a fourth swab. An estimate of the precision attaching to the predicted number is unobtainable, and the number of three (4%) can be considered to be only very approximate.

Discussion.

Other investigators have found that three laryngeal swab cultures are approximately equal to one gastric culture. The relative efficiency of the two methods has not been examined in this investigation. However, the results obtained with laryngeal swabs (from patients without sputum) have been compared with those obtained from routine sputum cultures of out-patients with sputum. Although sputum is admittedly superior material for culture than either gastric aspirate or laryngeal swabs, the results of sputum culture were only 5·9% superior to the results of culture of laryngeal swabs. From this comparison there seemed no reason to doubt the claims of other investigators concerning the relative effectiveness of laryngeal swab cultures.

The convenience of laryngeal swab culture compared with gastric culture is manifest. The patient does not have to be fasting, so that specimens can be taken at any time and further visits are reduced. The investigation is preferred by patients who dislike "swallowing the snake", and staff no longer have to set up a special tray. Laryngeal swabs are quicker to take, and the laboratory technique is simpler than for gastric culture. The method lends itself for use by general practitioners, who can take the swabs, inoculate the media, and then send the bottle through the post to the central laboratory, the whole procedure requiring a minimum of time and trouble.

The only objection has been the implied necessity of taking the multiple swabs on different days, on the theoretical grounds that there would be a progressive reduction in bacteria-rich material after repeated swabbing. This necessity would make the procedure impracticable for out-patients. Our results establish that there is no significant disadvantage in taking three swabs at the same session. Therefore it would appear that laryngeal swab cultures are the method of choice for out-patient investigation of patients without sputum.

It has been estimated that examination of a fourth swab would increase the positive cultures by approximately 3% to 4%. Therefore it is considered well worth while increasing to four the number of swabs taken at each session.

Summary.

1. Three laryngeal swab cultures have been reported to be equal to or better than one gastric culture.

2. It has been shown that triplicate swabs taken at one session are not inferior to three swabs taken on successive days, and each swab has an equal chance of producing a positive culture.

3. It has been estimated that the addition of a fourth swab would provide a further 3% to 4% of positive results, and its use would therefore appear warranted.

4. Laryngeal swabs are a valuable and simple means of obtaining material for culture from patients without sputum and are preferable to gastric culture for out-patients.

Acknowledgements.

We are indebted to Sister B. Doherty, who has taken all the swabs analysed in this study. This article is published with the permission of the Chairman of the Repatriation Commission.

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Addendum.

Since the above was written, a recent article by Wallace, Ross and Schiller (1955) has appeared on the use of alginate swabs. The authors used a series of four swabs, and their results show that 4% of their positive findings were produced by the fourth swab. This would appear to provide practical confirmation of the theoretical conclusion drawn from our figures.

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Reports of Cases.

THERAPY OF HUMAN TORULOSIS WITH ACTIDIONE AND "CONTRAMINE": A REPORT ON TWO CASES.

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THE cases of torulosis[1] seen at this hospital prior to 1946 have been discussed by Cox and Tolhurst (1946), and since that time there have been six cases. Several will be reported by Smithurst (1955). Two are discussed here, both patients having pulmonary and central nervous system involvement, and both being treated with "Contramine" and actidione.

"Contramine" (diethyl-ammonium-diethyl-dithio-carbamate) was found to act on *Torula histolytica in vitro*.[2] It has previously been used in *herpes zoster*.

Actidione, an antibiotic extracted from *Streptomyces griseus* cultures (Whiffen *et alii*, 1946), has strong antifungal properties, which include activity against *T. histolytica*. Carton (1952) reported a series of cases of torulosis treated with the drug, and others have used it (Evans and Herrell, 1952; Wilson and Duryea, 1951). However, sufficient clinical data have not yet been accumulated to give decisive evidence of the value of actidione in therapy or of the dosage required. This paper attempts to elucidate these problems.

Case 1.

A., a housewife, aged forty-four years, born in Tasmania but resident in a Melbourne suburb for thirty-five years, was admitted to hospital on October 9, 1953. Fifteen months previously her chest had been radiologically examined during a mass survey and the film regarded as normal. Three months before her admission to hospital, she noticed difficulty in climbing steps—her knees would suddenly give way, and at the same time she experienced a sharp stabbing pain in the right side of the chest, just below the shoulder blade. This pain was present intermittently for several days and was worse with sneezing and coughing, and she sought a further X-ray examination. This microfilm was queried, and larger films suggested the presence of a rounded mass, one inch in diameter, in the right lung. Five weeks prior to her admission to hospital she developed headache, severe and stabbing in both temporal regions; it lasted for a few minutes only and recurred over the next few days. It then became constant and generalized, often keeping her awake at night. At first it was moderately severe, but it increased in intensity until one week prior to our examining her; it then abated a little, but after a few days became particularly severe and was associated with nausea and vomiting. As a result of questioning it became apparent that her general health had been poor for several months, her appetite had been bad and she had lost weight. She had had for several years an unproductive cough associated with heavy smoking. Soon after her suspicious X-ray examination, the cough became productive, the sputum often being streaked with blood. The amount of sputum diminished after a month, and at the time of her admission to hospital she found difficulty in producing a specimen. For five weeks she had noticed that she was unable to read fine print. For a week she had been seeing double when she looked to the right. Her husband confirmed this story, and had not noticed any alteration in the patient's behaviour or memory.

On examination of the patient, she was drowsy but easily aroused, and became cooperative and attentive. Her memory was good and she was well orientated in time and place. There was no abnormality of the cardio-vascular system, and the only finding in the chest was the presence of a few basal crepitations on both sides. There was slight neck stiffness, and Kernig's sign was doubtfully present. Full clinical examination of her central nervous system revealed only nystagmus and diplopia; the nystagmus was horizontal, present on full lateral deviation to right and left; the diplopia suggested right lateral rectus paresis. The deep reflexes were brisk and the plantar reflexes flexor in type.

No lesion was seen in her skull on radiological examination, the pineal gland not being identified. X-ray examination of the chest confirmed the previous findings—a rounded mass, one inch in diameter, of more or less homogeneous but relatively slight radio-opacity being present in the paravertebral zone of the base of the apical segment of the lower lobe of the right lung. Electroencephalography gave no evidence of a focal lesion; bilateral high voltage δ wave activity, maximal in the frontal regions, frequently disturbed the record.

Lumbar puncture was performed. The cerebro-spinal fluid was faintly yellow and at a pressure of 240 millimetres of cerebro-spinal fluid, and contained 110 polymorphonuclear cells, 510 lymphocytes, 20 monocytes and 10 erythrocytes per cubic millimetre. Torulæ were also seen. The protein content was 90 milligrammes, the chloride content 720 milligrammes (as sodium chloride), and the sugar content 75 milligrammes, all per 100 millilitres. Torulæ were grown on culture.

Several sputum specimens were examined and torulæ were seen. No acid-fast bacilli were seen, and a guinea-pig which was inoculated did not develop tuberculosis. Liver function tests were performed and the prothrombin level was found to be 100%. The serum protein contents were as follows: total 6·6 grammes *per centum*, albumin 4·9 grammes *per centum*, globulin 1·7 grammes *per centum*. The cephalin flocculation test produced a negative result, and the serum bilirubin content was less than 0·25 milligramme per 100 millilitres.

The patient's urine contained no protein, the blood urea content was 35 milligrammes per 100 millilitres and the urea clearance after urea had been given (Fowweather) was 54% of the average normal figure. The white cells numbered 8000 per cubic millimetre, with normal proportions of various types. The hæmoglobin value was 13·0

[1] We shall refer to the infection caused by *Cryptococcus neoformans* or *Torula histolytica* as torulosis.

[2] The drugs "Paludrine", mepacrine, dibromo-propamidine and BAL were also found to be active *in vitro*. "Contramine" and "Paludrine" were found inactive in animal experiments. Small doses of "Contramine" were given over a long period to a private patient of Dr. L. B. Cox; its value could not be assessed because the patient refused investigation, but he either responded to "Contramine" or experienced a prolonged natural remission.

grammes per 100 millilitres, and the red cells were normal in appearance, occasional stippled cells being seen.

The prognosis was considered to be poor. Consequently a course of "Contramine" with large doses was decided upon. The second lumbar puncture on October 14, 1953, gave results similar to the first. The patient was given "Contramine" intramuscularly, 0·125 gramme twice a day for one day, 0·25 gramme twice a day for the second and third days, and thereafter 0·5 gramme twice a day. Some hours after the second injection of 0·5 gramme of "Contramine" a series of generalized fits occurred. Twelve hours later the patient was reasonably alert, the right lateral rectus paresis was more evident, she had coarse horizontal and vertical nystagmus, and movements of her limbs were slightly incoordinate. There was paresis of the left side of the face. It was decided to suspend therapy for several days, but no more fits occurred and therapy was recommenced with a dosage of 0·5 gramme twice a day, as her headache was now increasing in intensity and she was becoming slowly disorientated.

A further fit occurred after two doses, and therapy was suspended for twenty-four hours, but recommenced because the patient's general condition was rapidly deteriorating. Her visual acuity, which had been normal, diminished greatly during the next forty-eight hours, and both pupils became fixed and dilated. There was a bilateral lateral rectus palsy, and the deep reflexes could not be elicited.

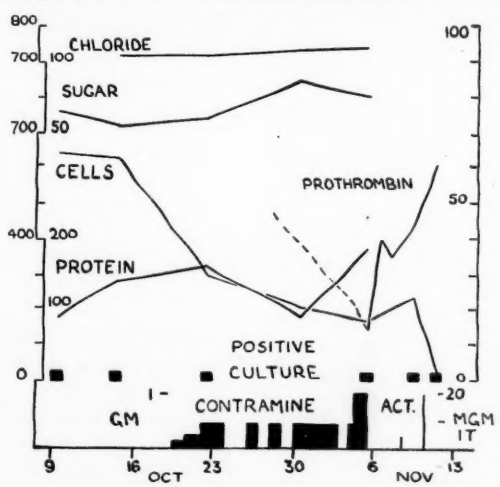

FIGURE I.

Drug therapy and laboratory results in Case I. Cerebrospinal fluid results. Chloride (as sodium chloride), sugar and protein as milligrammes per 100 millilitres; cells as number per cubic millimetre. Prothrombin level as percentage of normal.

After four days of intensive therapy it became apparent that, although her condition was deteriorating, her cerebrospinal fluid findings had improved slightly. However, attempts at culture were still successful, and in several specimens torulæ were seen. Thus at this stage, November 2, 1953, she had had nine grammes of "Contramine". She was confused, drowsy and disorientated in time. She was noisy and irrational at night and needed morphine or "Physeptone" to control her headache. She could tell light from dark with both eyes, but she could not count fingers. The optic disks were flat and slightly paler than before. Both pupils were dilated and failed to react to light. No nystagmus was noted; the external ocular movements were very incomplete; lateral movement on both sides was absent; elevation and depression were incomplete and unsustained. The corneal reflexes were brisk, and there was no evidence of involvement of the trigeminal or facial nerves. She was too uncooperative for hearing tests. There was no dysphagia, the palatal and pharyngeal reflexes were brisk, and the tongue was protruded in the mid-line without tremor. There was no specific defect of the motor system apart from general weakness, diminished tone in all limbs and some incoordination during the performance of rapid movements. Sensation was hard to assess; she complained of numbness and heaviness in both hands, but all forms of sensation seemed intact. All deep reflexes were hard to obtain, the superficial abdominal reflexes were absent, and plantar reflexes were flexor in type.

It was thus evident that besides mental deterioration there were signs of basal meningitis or brain stem involvement. In view of this we decided to increase the dose of "Contramine", and consequently for two days she received one gramme twice a day. However, only two doses had been given when it was noticed that she was bruising very easily with minimal trauma. A prothrombin estimation gave the value of 20%, the cephalin flocculation test producing a negative result. Large doses of vitamin *K* were given, and after a further eighteen hours, when a prothrombin value of 15% was obtained, "Contramine" therapy was stopped. The next day the patient was having difficulty in swallowing, her voice was loud and unmodulated, and she had a fine, generalized purpuric rash. At this stage lumbar puncture showed the pressure of cerebrospinal fluid to be over 300 millimetres. The cell count was 174 per cubic millimetre, and the protein content was 180 milligrammes per 100 millilitres. Torulæ were both seen and cultivated in greater numbers than before. It thus appeared that "Contramine" had had no beneficial effect, and therapy was discontinued. At no time had "Contramine" been detected in her blood or cerebro-spinal fluid. Over the next few days the daily prothrombin estimation slowly rose, the bruising tendency and the rash disappeared. The cephalin flocculation test result became positive three days after therapy ceased, but three days later reverted to negative.

As her condition was much worse we decided to give actidione intrathecally, the quantity necessary for intramuscular use not being available. Consequently, five milligrammes were given diluted in two cubic centimetres of saline on the first day. Over the next two days her condition rapidly became worse. Twenty milligrammes of actidione were given intrathecally on November 11, 1953, and on November 12 she died suddenly. The cell count on November 11 was low, 24 cells per cubic millimetre being counted. However, many torulæ were seen and grown on culture.

For the post-mortem findings we are indebted to Dr. R. McD. Anderson. The autopsy was performed nine hours after death. The heart and vessels, and the hæmatopoietic and genito-urinary organs were normal. In the chest the upper part of the lower lobe of the right lung was adherent to the posterior chest wall over an area one inch in diameter. Under this adhesion was a circular mass, one and a half inches in diameter. Section through the lung revealed a well encapsulated mass with a honeycomb appearance. On microscopic examination the mass contained many torulæ, a few lymphocytes and an occasional giant cell. The capsule was of fibrous tissue with many small blood vessels. The surrounding lung was normal.

The brain was normal in size and shape. The pia-arachnoid contained clear cerebro-spinal fluid, and apart from a minor degree of "milkiness" in the sulci there were no signs of meningitis. Coronal sections were cut through the brain; two honeycomb areas (a quarter of an inch in diameter) were found in the right putamen. Microscopic examination showed that the subarachnoid space contained many torulæ, associated with a minor degree of round-cell infiltration. Giant cells were a prominent feature, and some of these contained torulæ. In every section of brain and brain stem examined, small foci containing torulæ and small round cells were found; some of the torulæ were budding.

On macroscopic examination the liver appeared normal; histological examination showed minor fat deposition in the cells. The rest of the digestive organs were normal, apart from scattered petechial hæmorrhages of varied size in the mesentery. These findings, together with a few bruises on the body, especially around sites of injection and lumbar puncture, were the only evidence of the previous bruising tendency.

Comment.

In the initial assessment of this case we regarded the prognosis as hopeless, and "Contramine" was used in larger doses than we had used before. The patient was deteriorating rapidly, and it is difficult to ascribe any of her nervous manifestations to the form of therapy used. However, it is quite definite that the low prothrombin level with the associated bruising tendency was a direct consequence of the "Contramine". This severe toxic manifestation, together with failure to arrest the organism, shows that the drug is of no value in torulosis.

Case II.

B., a gardener, aged sixty-one years, was transferred from Cairns on June 16, 1953, the diagnosis of torulosis having already been established there (Horsfall and Geaney, 1955). This patient presented primarily with headache of four weeks' duration, and on examination he was drowsy but easily roused, becoming cooperative. His headache was frontal and mildly persistent. There was a moderate degree of neck stiffness, Kernig's sign was present, and full clinical testing of the central nervous system failed to reveal any other abnormality.

Lumbar puncture produced faintly yellow fluid at a pressure of 110 millimetres of fluid. The fluid contained 360 milligrammes of protein, 690 milligrammes of chloride (as sodium chloride) and 30 milligrammes of sugar per 100 millilitres. There were 293 cells present per cubic millimetre—218 lymphocytes, 68 polymorphonuclear cells and six mononuclear cells. Torulæ were seen and cultivated from the fluid. Plain X-ray films of the skull and chest failed to show any abnormality. A blood examination showed the hæmoglobin value to be 13·6 grammes per 100 millilitres; the white cells numbered 10,000 per cubic millimetre, 5600 being neutrophile cells, 2600 lymphocytes, 1100 monocytes and 700 eosinophile cells. The electroencephalogram contained slender evidence of a left central parasagittal destructive process.

Whilst a supply of actidione was being obtained we decided to try a course of "Contramine", the patient's strain of torula being sensitive to 12·5 microgrammes per millilitre. Over the next forty days a total dose of 2·75 grammes of "Contramine" was given intramuscularly, an average of 125 milligrammes every second day. The largest single daily dose used was 250 milligrammes. Over these forty days the patient's condition improved considerably: an initial pyrexia of from 99·5° to 100° F. settled down, and he lost his headache and became fully alert and ambulant. The cell content of the cerebro-spinal fluid decreased to a total of approximately 100 per cubic millimetre, there being a parallel fall in the number of lymphocytes and polymorphonuclear cells. The protein level fluctuated considerably in the 200 to 300 milligrammes per 100 millilitres level; the sugar and chloride levels rose to within normal limits. Torulæ were frequently seen and were cultivated from nearly every specimen (Figure II, June to July).

A second electroencephalogram showed an over-all improvement in the record.

However, at no stage, at various time intervals after injection, could "Contramine" be detected in either blood or cerebro-spinal fluid. It was therefore concluded that the clinical improvement was due to a natural remission rather than to therapy, and as a supply of actidione had arrived, it was decided to start using it forthwith. The patient's organism was found to be sensitive to five microgrammes per millilitre.

Since few reports had then been published, it was difficult to decide what dose to use. There was no reaction to a test dose of one milligramme, and after this 20 milligrammes were given intramuscularly every six hours for twenty-one days.

The initial toxic manifestations were found to be nausea and vomiting, maximal about three-quarters of an hour after injection; these were well controlled by giving orally 0·5 grain of phenobarbital and 50 milligrammes of "Andramine" one hour prior to the injection. Ataxia was not found. Four days after the start of actidione therapy slight confusion and disorientation occurred, but these fluctuated from time to time and did not interfere with the patient's ambulant state.

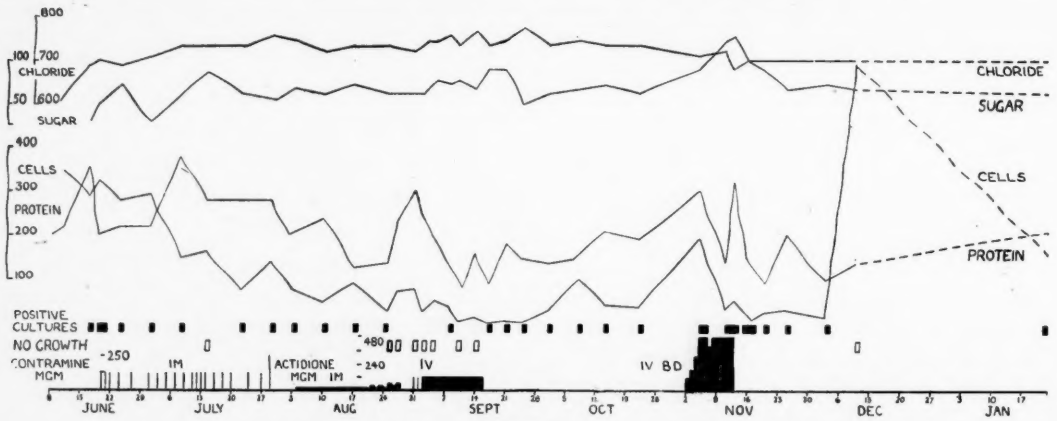

FIGURE II.

Drug therapy and laboratory results in Case II. Units of measurement as in Figure I.

Throughout the course regular estimations of actidione in the blood and cerebro-spinal fluid were performed. At no time was an adequate level demonstrated. In view of this, it was decided to increase gradually the dose of actidione. By increasing the dose in steps of 20 milligrammes, it was found possible to give 120 milligrammes intravenously twice a day without untoward effect; some nausea and vomiting and slight confusion were found, but responded to phenobarbital and "Andramine" as before. The blood levels were determined, and on September 2, 1953, a course was started consisting of 120 milligrammes given twice a day for fourteen days. The 120 milligrammes of actidione were diluted to a total volume of 20 to 25 millilitres with isotonic saline and given over five to ten minutes. By so diluting the solution, we were able to use one vein three or four times before mild thrombophlebitis prevented its further use. Too rapid administration of the drug produced excessive nausea and vomiting.

Three days after the course started, it was noticed that the patient's confusion was increasing; but this fluctuated, and four days later he was considered to be a normal man of sixty-one years, there being no evidence of intellectual deterioration. However, in the next few days he became dreamy and carefree, preferring to stay in bed all day. He was slow in responding to questions and showed increasing confusion, which lasted all day towards the end of the course. Psychometric evaluation revealed evidence of

retardation, confusion, perseveration and deterioration of intellectual function.

During the early period of this course his confusion was more apparent in the early afternoon, the morning dose of actidione having been given at 10 a.m. The highest blood concentration of the day was demonstrated just after its administration, and at the time when the confusion was maximal—approximately 2 p.m.—only a small amount of actidione was found in the blood.

During this course frequent cerebro-spinal fluid examinations were made. The protein level fell, and the total number of cells dropped below 20 per cubic millimetre; but torulæ continued to be cultured from most specimens (Figure II, September). The actidione content of the cerebro-spinal fluid and blood was estimated at various time intervals after injection. Speciments of urine were examined in an attempt to account for actidione excretion. The collection of these specimens was made difficult by the patient's mental state, and it is doubtful whether we ever collected the full quantity.

During the ten days after the course finished, frequent psychometric evaluations were performed; his responses gradually improved, he wanted to get out of bed and was able to look after himself completely. Ten days after actidione therapy ceased, he was considered to have an organically determined dementia of moderate degree; however, it was difficult to distinguish this from disability due to his age. An electroencephalogram performed during the height of his confused state showed a change in the fundamental quality of his record, but a week later there was considerable improvement.

He was consequently allowed to return home, where his family found that he was not as alert as before and his memory was poor, especially for recent events. We considered the over-all improvement in the clinical condition and cerebro-spinal fluid findings to be a natural remission. From the actidione assays which were performed, it was concluded that with the dosage used a satisfactory level was not reached. A further course of actidione had then to be considered. Against the known toxic manifestations we had to balance the fact that the patient had an infection which would eventually be fatal.

Over the next month the patient was examined regularly and frequent lumbar punctures were performed. Mentally he improved slightly, and no neurological abnormalities were found, but he again started to have headaches. Over this time also the cerebro-spinal fluid cell count rose slowly to a maximum of 100 per cubic millimetre, and the protein content to 200 milligrammes per 100 millilitres.

We therefore considered that there was adequate evidence that the disease process was advancing after a temporary remission, and decided that a further course of therapy was not only desirable but urgent. The dosage to be used was planned beforehand, the previous assays being used as a basis. It was decided to reach 480 milligrammes every twelve hours in increasing dosages, and to keep at the maximum level as long as possible. The actidione (10 milligrammes per millilitre) was diluted so that 480 milligrammes were given in 200 millilitres of saline over ten to twenty minutes. Later in the course an intravenous infusion of saline containing 5000 units of heparin per litre was set up, the diluted actidione being added to the barrel every twelve hours, and the full dose being given again within twenty minutes. This not only conserved veins, but served as a means of giving the patient fluid.

Nausea and vomiting were countered with phenobarbital, 0·5 grain three times a day, and "Dramamine", 100 milligrammes one hour prior to injection. However, in spite of these, vomiting was troublesome early in the course when the patient was having a solid diet. Later, when he was depending on a fluid diet and the intravenous infusion, vomiting was infrequent.

The maximum dose of 480 milligrammes twice daily was built up in three days. Over this time he became mildly disorientated and further intellectual impairment was demonstrable. Over the next seven days the same dose was given. On the fourth to seventh days of this regime he became progressively drowsier, uncooperative, disorientated and at times hallucinated, preferring to lie passively in bed. He became incontinent of urine and fæces, and his electroencephalogram showed more slow activity than was previously present.

Because of the apparent gross deterioration of intellectual capacity, the intravenous actidione therapy was stopped. However, up to two days before this, torulæ were still cultivated from the cerebro-spinal fluid, and estimations of actidione showed that the blood and cerebro-spinal fluid level was still insufficient for adequate therapy.

At this time the patient in Case I was being treated, and we therefore had some preliminary experience in the intrathecal use of actidione. Consequently (November, 1953) it was decided to start intrathecal therapy; 10 milligrammes were given the first day, then 20 milligrammes daily for five days, the dose being diluted with two millilitres of isotonic saline. The first two days of this form of therapy coincided with the last two on which intravenous therapy was used.

After the cessation of intravenous actidione therapy, the patient's mental condition was stationary for several days and then slowly improved. One week later it was considered that his cognitive processes were still very grossly impaired. The week after this he was greatly improved, but still moderately disorientated in time and place. However, after a further week he was considered to be substantially back to his last pre-treatment condition. Although he was cooperative, his spontaneous activity was minimal.

Altogether it was four to five weeks before he was able to look after himself completely. His convalescence was complicated four days after intravenous therapy ceased by bilateral thrombosis of the femoral artery affecting predominantly the left leg. This responded to conservative treatment without any evidence of tissue necrosis.

Lumbar puncture findings throughout the course showed some improvement in the overall picture. The cell count in the cerebro-spinal fluid fell to 10 lymphocytes per cubic millimetre at the cessation of the intrathecal therapy. The protein content was 90 milligrammes per 100 millilitres. During the next four weeks the cell count remained low, the protein content fluctuating between 100 and 200 milligrammes per 100 millilitres. However, from all specimens torulæ were grown on culture.

There again was no evidence of renal or hæmatopoietic damage. Hepatic function was assessed by regular prothrombin, cephalin flocculation and serum protein estimations. The result of the cephalin flocculation test remained negative, the serum protein contents were unaltered, but during the course the prothrombin level fell to 30%, and over the next month fluctuated between 50% and 70%. There was no other evidence of liver damage.

Complete reexamination of the patient one month after the end of therapy failed to reveal any general or neurological abnormality apart from very slight dementia. He was examined again one month later, when there was no clinical evidence of a focal lesion of the central nervous system, and his mental state had improved slightly; this impression was confirmed by his wife.

The patient was again admitted to hospital on February 12, 1954—eight months after his original admission. He had experienced fairly severe headache for about seven days, and one hour prior to his admission he had a major epileptic attack, being unconscious for twenty minutes. No evidence of unilateral predominance was noticed by his relatives.

On his admission to hospital he was conscious and cooperative, and examination gave no evidence of any central nervous system abnormality. There was no neck or spine stiffness. He was given phenobarbital, 0·5 grain, and "Dilantin", 1·5 grains three times a day, and no further attacks occurred.

There was no clinical or radiological evidence of a pulmonary lesion. His electroencephalogram gave no evidence of epileptic activity, but there was an increase in the predominantly left-sided slow activity that had been

noted previously. It was hard to say after rapid testing whether he had deteriorated mentally any more than when we had seen him last. However, it became apparent after a few days that there had been some more deterioration, but this was slight.

He remained in hospital until his death five months later. His mental state deteriorated rather rapidly in the first month; he became incontinent of urine and fæces and only occasionally recognized his relatives. From time to time lumbar puncture was performed; torulæ were always cultivated from the cerebro-spinal fluid, the cell count remained below 60 per cubic millimetre, and the protein content remained above 150 milligrammes per 100 millilitres. The electroencephalographic readings became more definite with evidence of slowly progressive destructive processes in both hemispheres, maximal in the left.

His general condition deteriorated rapidly over the last month, and he died on July 9, 1954.

Apart from central nervous system lesions, the post-mortem examination revealed a small toruloma in the middle of the upper lobe of the right lung. Externally the brain appeared normal, but horizontal sectioning showed two encapsulated gelatinous masses in the right frontal lobe, the larger being the size of an inch sphere. These gelatinous lesions contained numerous torulæ, some of which were "calcified". Examination of the meninges revealed a moderate infiltration of small round cells, and torulæ were present only in small numbers.

Bacteriological Data.

Organisms from both patients were typical *T. histolytica*, pathogenic for mice. Both strains were sensitive to 12·5 and resistant to 6·0 microgrammes of "Contramine" per millilitre; both were sensitive to 5·0 and resistant to 2·5 microgrammes per millilitre of actidione. Eight strains from former patients showed the same sensitivity to actidione as these, but two others were inhibited by 0·3 microgramme per millilitre. Cultures grown from cerebro-spinal fluid taken from the patient in Case II after his second and third courses of actidione therapy were unchanged in sensitivity. The organisms were resistant to more than 100 microgrammes per millilitre of polymyxin B, and no synergism could be demonstrated between actidione and polymyxin B with this strain (Carton, 1952).

The sensitivity of strain B. was determined more exactly by the use of standard drops of dilutions of culture placed on the surface of Sabouraud agar plates containing different concentrations of the drug. The endpoint (no visible colonies) lay between 2·5 and 5·0 microgrammes per millilitre in each case. The mean numbers of colonies per drop on the control plates were 3·44, 1·78 and 0·88 in the case of the three highest dilutions (50 replications), and the endpoints were calculated to be 4·2, 4·0 and 3·1 microgrammes per millilitre respectively.

Determinations of the concentration of drug in body fluids were carried out by diluting one millilitre of fluid in twofold steps with glucose tryptic broth containing one-tenth of its volume of three to seven day old cultures of *Saccharomyces pastorianus*. This organism was sensitive to 0·04 and resistant to 0·02 microgramme per millilitre of actidione. Incubation was at 30° C. Preliminary tests showed that normal serum, cerebro-spinal fluid and urine did not destroy actidione in the time necessary to set up the tests. However, undiluted cerebro-spinal fluid did not support growth of the organism, and quantities smaller than 0·08 microgramme per millilitre could not be detected.

Growth rates were determined in glucose tryptic broth. Dilutions were of the order of 0·5 millilitre in five millilitres, and standard drops (63 per millilitre) of these were plated on Sabouraud agar. Five replications were the minimum number.

Discussion.

"Contramine."

No benefit, but, on the contrary, serious toxic effects, were seen from the use of "Contramine". There were no indications for its further trial.

Actidione.

Again, no beneficial effects were demonstrated from actidione; nausea and vomiting were observed and controlled, mental deterioration was seen in accentuated form, and another toxic effect—a fall in prothrombin level—was observed for the first time. However, the drug cannot be dismissed, since it has been reported as curative (Wilson and Duryea, 1951).

It was found that fifteen minutes after the intramuscular injection of 40 milligrammes of actidione, the blood contained 0·64 microgramme per millilitre. This concentration was maintained for a short time and then fell. The concentration in the lesion cannot be determined; presumably it is less than the blood concentration. Though antibiotics may be concentrated by some tissues, it is not to be expected that this power is retained by the dead cells in a lesion. Therefore a concentration in the blood lower than that to which the organism is sensitive *in vitro* indicates a dose too small to be effective. A course of treatment at this dosage was tried and the cerebro-spinal fluid remained infected.

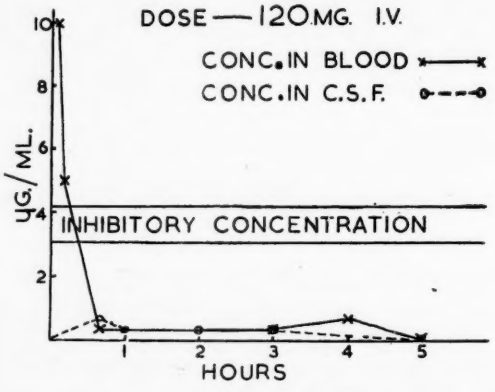

FIGURE III.

Concentration of actidione found in the blood and cerebro-spinal fluid after a dose of 120 milligrammes given intravenously, expressed as microgrammes per millilitre.

The results of testing after 40, 60 and 80 milligrammes had been given intravenously indicated the necessity of raising the dose still further. All results were in conformity with a curve of the shape illustrated in Figure III, and later determinations were timed to measure the height of the plateau. If the preceding transitory peak is disregarded for the moment, it may be seen that the blood level resulting from a dose of 120 milligrammes given intravenously, 0·32 microgramme per millilitre, still was much less than the inhibitory concentration. Larger doses raised the level, but even 480 milligrammes given intravenously produced in the blood a concentration of only 1·28 microgrammes per millilitre during this phase. This could not be expected to produce the desired result and was in fact found not to do so.

The highest level found in any one of a series of tests of the cerebro-spinal fluid was in the earliest specimen, collected forty minutes after administration of the drug. Evidently actidione easily enters the cerebro-spinal fluid, and the amounts found were equal to or a large fraction of those in the blood at the same time. A concentration of 1·28 microgrammes per millilitre was found one and a half hours after the injection of 480 milligrammes, but torulæ were cultivated from this specimen as from most others.

Five hours after the intrathecal injection of 20 milligrammes of actidione, a concentration of only 10 microgrammes per millilitre was found. Two specimens, one taken twenty-four hours and the other twenty-eight hours after the intrathecal injection of 20 milligrammes, contained no actidione, and torulæ were cultivated from them.

Intrathecal therapy has general disadvantages as well as the toxic effect (intractable nerve root pain) discussed by Carton (1952).

At times there were very few torulæ in the cerebro-spinal fluid. It appeared possible that the drug might be more active in these circumstances. Therefore more precise tests were made. These showed that reducing the inoculum in a sensitivity test from 2000 organisms to one organism reduced the concentration of the drug needed to inhibit growth only from a figure close to but less than five microgrammes per millilitre to 3·1 microgrammes per millilitre. This phenomenon, which is less in the case of actidione than in the case of some other drugs, would have a negligible effect.

A series of negative results on attempted culture was encountered (Figure II). These specimens were inoculated on Sabouraud slopes or into tryptic broth tubes in one millilitre quantities as usual, and the number of tubes showing growth (expressed as a fraction of the number inoculated) is given below, starting at August 10 and ending at

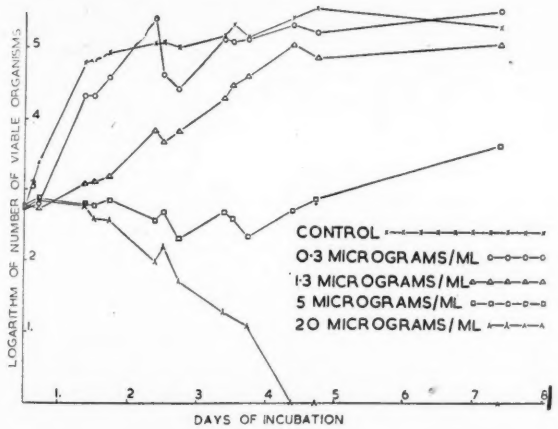

FIGURE IV.

The numbers of viable *T. histolytica* organisms found after various time intervals in cultures containing various quantities of actidione.

September 21: 1/5, 2/5, 1/4, 0/4, 0/2, 0/5, 0/4, 0/2, 2/7, 0/6, 0/4, 3/6, 6/8. The random distribution of small and variable numbers of organisms in a volume of fluid suffices to explain these results. The specimen of September 8, which gave the positive result in the middle of this series, contained as much actidione (0·64 microgramme per millilitre) as the four preceding it. This experience shows again the necessity of cultivating large volumes of cerebro-spinal fluid on numerous occasions before concluding that it is sterile.

Attention has so far been directed to the second part of the curve shown in Figure III, but if it was found that some feasible concentration of actidione killed the torulæ in an hour or two, then the first part of the curve shown in Figure III would become important, and a trial would be necessary of some form of therapy intended to take advantage of the short period of high concentration in the blood which follows an injection.

However, Figure IV shows that even 20 microgrammes of actidione per millilitre took five days to kill the organisms at 30° C. A similar experiment in which the action of five microgrammes per millilitre at 37° C. was compared with its action at 30° C. showed that while the torulæ multiplied more slowly at the higher temperature, the drug, though more effective, still took three days to kill the organisms. This concentration could be maintained in the patient's blood-stream, even after the largest doses, for less than an hour. Increasing the temperature to 39° C. did not add further to the effect of the drug. Therefore hyperthermia, which has been suggested as a method of treatment, cannot be expected to enhance actidione therapy to any great extent.

Because of the patient's mental state, attempts to follow completely the excretion of the drug in the urine failed. However, the amount recovered (13 milligrammes out of 600 injected) was so small that it is safe to conclude that the bulk of the drug is excreted in an inactive form.

No evidence was found of any accumulation of active drug in the blood or cerebro-spinal fluid upon continued administration. The clinical and laboratory observations are explained by the hypothesis that actidione is largely destroyed in the body, and the products are inactive toward torulæ, toxic to the patient and slowly excreted.

Conclusions.

Four hundred and eighty milligrammes of actidione appears to be too large a dose to use safely, yet it was not enough to affect the progress of the disease in this patient. The drug has a fungistatic action, and effective concentrations could not be maintained; rapidly fungicidal concentrations could not be attained.

Nevertheless, we do not think that actidione should be abandoned. The drug quickly appeared in the cerebro-spinal fluid in concentrations approaching the blood level. This patient's organism was moderately resistant to the drug; but Carton (1952) has reported and we have observed strains much more sensitive. The sensitivity of the organism remained unchanged after treatment. Finally, it cannot be concluded that actidione always disappears from the blood and cerebro-spinal fluid so rapidly as in this case.

Summary.

1. The history, treatment and investigations in two cases of torulosis involving the lung and central nervous system are reported.

2. "Contramine" was found to be ineffective in treatment.

3. Actidione was ineffective, and possible reasons for its failure are advanced.

4. Actidione has a predominantly fungistatic action. Even toxic doses produced only low concentrations in blood and cerebro-spinal fluid relative to the moderate sensitivity of these two strains of torulæ.

Acknowledgements.

We wish to thank Dr. John A. Game, Acting Honorary Neurologist to the Alfred Hospital, for his advice and for permission to publish details of Cases I and II, and Dr. L. B. Cox, Honorary Neurologist to the Alfred Hospital, for permission to publish details of his case. Associate Professor D. W. McElwain has by his help and interest aided us considerably in the psychometric aspects of these cases. The Upjohn Company of Kalamazoo, Michigan, generously supplied the actidione, and Dr. Harold R. Reames of that company gave ready cooperation. We are obliged to Dr. Eileen Fisher for locating the test organism, *Sacc. pastorianus*. Acknowledgements are due to Dr. R. McD. Anderson and Dr. Ian Robertson, who carried out the post-mortem examinations, and to Mr. A. N. Jones, who gave advice on and performed the calculations of the experiment on the variation of endpoint.

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Reviews.

La Pensée Morale en Médecine: Premiers Principes d'une Ethique Médicale. By W. Riese, M.D., with a preface by Henri Baruk; 1954. Paris: Presses Universitaires de France. 9" × 6", pp. 94. Price: 420 francs.

THIS is a slight philosophical essay on the evolution of the doctor-patient relationship. Before there was any real knowledge of disease and treatment there were magic and witch-doctors, and the relationship between practitioner and patient was that of charlatan and victim. With the dawn of knowledge and the realization of the significance of symptoms and of the efficacy of empirical treatment came the concept of the patient as an individual and of the doctor's personal relationship with and responsibility for his patient; then came the need for research into ætiology, and the responsibility of the doctor to increase and extend his knowledge so as to give more and better service to his patients, and the doctor-patient relationship became ever more intimate and responsible, with the patient's individual and personal welfare the paramount consideration. But when the concepts of preventive medicine emerged, the doctor was faced with a moral problem of some perplexity, in that the personal welfare of his patient might often need to be subordinated to the general welfare of the community. Professor Riese rationalizes the conflict of ideas by explaining that where the State requires certain things done which conflict with the individual's wishes, nevertheless the State represents the individuals who compose it, and therefore the doctor can impose the requirements of preventive medicine upon his patient with a clear conscience.

The author does not extend his philosophical ideas to the Welfare State, or to the practice of medicine in totalitarian States, so that the most important problems are left untouched.

Bedside Diagnosis. By Charles Seward, M.D., F.R.C.P. (Edinburgh), with a foreword by Henry Cohen, M.D., D.Sc., LL.D., F.R.C.P., F.F.R.; Third Edition; 1955. Edinburgh and London: E. and S. Livingstone, Limited. 7½" × 5", pp. 432, with a few text figures. Price: 18s. 6d.

THIS delightfully written book, having run through three editions, besides being translated into Spanish and Portuguese, all in a space of six years, must now be classified as a medical best-seller. Despite the fact that so much detail is confined in a comparatively small volume, yet because of the practical approach to each topic, the value of the book to all practising doctors and students is thus doubly enhanced. Each chapter is headed by the name of a clinical sign or symptom such as hæmaturia, dyspnœa, vomiting, jaundice, besides pain in all localities, and indeed the discussions on pain cover 102 pages out of the volume's total of 397. These distinct chapters provide a sound basis for tutors to use for their lectures, and all students will facilitate their approach to their clinical examinations by a careful study of it.

The book will prove invaluable to all doctors, young or old, who can derive herein much guidance which will assist them in solving the knotty problems with which all are suddenly confronted, either in the surgery or at the bedside. At a time when some doctors fill in forms, often needlessly, to order a spate of diagnostic tests, it is a real stimulant to read and recommend such a book as this, for it will certainly do much to prevent thoughtful clinicians, at least, from blissfully lapsing into a state of abulia.

Notes on Books, Current Journals and New Appliances.

Family Doctor. Published monthly by the proprietors, the British Medical Association, Tavistock Square, London, E.C.1. Sole agents for Australia and New Zealand: Gordon and Gotch (Australia), Limited. Subscription for twelve months: 20s. (sterling), including postage.

IN *Family Doctor* the approach to problems like cancer, squint, flat feet or divorce (some of the subjects in the October, 1955, issue) is simple, matter-of-fact, and consequently unfrightening and understandable; no harm and a lot of good should come from such an approach. The home-making supplement has good, practical articles, and there are plenty of useful and entertaining small pieces here and there. This is one of the really good family magazines.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Work of the Mental Nurse"; a survey organized by a Joint Committee of the Manchester Regional Hospital Board and the University of Manchester; 1955. Manchester: University Press. 8½" × 5½", pp. 164, with many illustrations. Price: 10s.

This is really a job analysis of the nursing duties in a mental hospital.

"Remedial Exercises for Postural Defects for Use in the Home and School", compiled by L. S. Rolleston; introduced in a revised form by T. Price, M.Ch.Orth.; 1955. Bristol: John Wright and Sons, Limited. 8½" × 5½", pp. 16, with 16 illustrations. Price: 2s. 6d.

A simple illustrated guide to the exercises used at orthopædic clinics affiliated to the Bath and Wessex Orthopædic Hospital.

"Dextran: Its Properties and Use in Medicine", by John R. Squire, M.D., F.R.C.P., J. P. Bull, M.D., W. d'A. Maycock, M.D., and C. R. Ricketts, Ph.D., F.R.I.C.; 1955. Oxford: Blackwell Scientific Publications. 8½" × 5½", pp. 92, with many illustrations. Price: 15s.

Deals with the chemistry of dextran, its behaviour in the body, its specification, clinical uses and experimental uses.

"An Introduction to Psychiatry", by Max Valentine, M.D., D.P.M.; 1955. Edinburgh and London: E. and S. Livingstone, Limited. 7½" × 5", pp. 306, with many illustrations. Price: 15s.

The author has attempted "to present psychiatry for the medical reader in such a way that it will be consistent with his training in applied biological science".

"Glaucoma: A Symposium Organized by the Council for International Organizations of Medical Sciences, Established Under the Joint Auspices of UNESCO and WHO", edited by Sir Stewart Duke-Elder; 1955. Oxford: Blackwell Scientific Publications. 9" × 5½", pp. 362, with many illustrations. Price: 37s. 6d.

The symposium was held in September, 1954, when the International Congress of Ophthalmology was held at Montreal and New York and was organized by the Council for International Organizations of Medical Sciences. The book contains the formal papers and discussions and is not to be regarded as a comprehensive text-book on the subject.

"Recent Advances in Neurology and Neuropsychiatry", by Sir Russell Brain, Bt., D.M. (Oxon.), P.R.C.P., and E. B. Strauss, M.A., D.M. (Oxon.), D.Sc., F.R.C.P., with the assistance of Denis Hill, M.B., F.R.C.P., D.P.M., Douglas Northfield, M.S., F.R.C.S., and David Sutton, M.D., M.R.C.P., F.F.R., D.M.R.D.; Sixth Edition; 1955. London: J. and A. Churchill, Limited. 8" × 5", pp. 322, with 46 illustrations. Price: 30s.

Entirely rewritten since the last edition appeared in 1945.

"Ophthalmology: A Textbook for Diploma Students", by Patrick D. Trevor-Roper, M.A., M.B., B.Chir. (Cantab.), F.R.C.S., D.O.M.S. (Eng.); 1955. London: Lloyd-Luke (Medical Books), Limited. 8½" × 5½", pp. 672, with many illustrations. Price: 75s.

Intended to cover the field of pre-clinical and clinical ophthalmology embraced by the London "Diploma in Ophthalmology". Any service it may offer to the undergraduate student, the F.R.C.S. candidate or the general practitioner "will only be incidental".

"The Medical Clinics of North America"; 1955. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. Cleveland Clinic, Scott and White Clinic. 9" × 6", pp. 326, with 190 illustrations. Price: £8 2s. 6d. *per annum* with cloth binding and £6 15s. with paper binding.

Consists of two symposia. The first is on diseases of the kidney and comes from the Cleveland Clinic Foundation and the Frank E. Bunts Educational Institute, Cleveland, Ohio; it comprises thirteen articles. The second symposium deals with endocrine disorders and endocrine therapy; it comes from the Scott and White Clinic, Temple, Texas, and consists of twelve articles.

The Medical Journal of Australia

SATURDAY, NOVEMBER 19, 1955.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

NONSENSE.

A little nonsense now and then
Is relished by the wisest men.

WHAT is nonsense? Nonsense is lack of sense, in the same way that disease is lack of ease. One of the occasions on which sober-minded and wise men will relish nonsense is likely to occur soon after they have had to confine their attention for a lengthy period to serious matters, academic or scientific, connected with their avocations. The suggestion, therefore, that, immediately after the concentrated effort of Congress, nonsense was a suitable subject for discussion, was welcomed. The man who cannot become light hearted and nonsensical now and again is to be pitied. It takes a wise man, we are told, to be a fool; but one who appears in the role of fool is not always a wise man. A serious person who can at will turn on a flow of nonsense has an enviable gift and is a joy to his companions. If the flow is so intense and enduring that it becomes a flood, the joy of companions ceases, the giver of the nonsense is dubbed a bore, and the quality of his serious utterances may be questioned. It is usual in some circles to ask whether a man (or woman) knows how to laugh in the right place; it is equally important to know whether he can make other people laugh in the right place. There are some happy souls who can make almost any occasion become "the right place". There comes to mind a medical man, highly skilled in his branch of study, who a year or two ago was president of one of the medical societies that meet from time to time in Australia. This man by a happy turn of phrase or even by a look or a gesture was able to combine the serious side of the gathering over which he presided with a light-hearted cheeriness. It was a joy to watch him. Once or twice his sense of fun was like the carbon dioxide in a soda water bottle when the cap is removed and in spite of himself he had to give way to mirth in which everyone joined—but the serious discussion was not checked. Perhaps the most celebrated piece of nonsense writing is credited to Samuel Foote (1854):

> So she went into the garden to cut a cabbage leaf, to make an apple-pie; and at the same time a great she-bear, coming up the street, pops its head into the shop. "What! no soap?" So he died, and she very imprudently married the barber; and there were present the Picninnies, and the Joblillies, and the Garyulies, and the grand Panjandrum himself, with the little round button at top, and they all played at the game of catch-as-catch-can till the gunpowder ran out at the heels of their boots.

Lewis Carroll (Charles Lutwidge Dodgson) will be called to mind by most of us as probably our best loved nonsense writer. None but Carroll could write:

'Twas brillig, and the slithy toves
Did gyre and gimble in the wabe;
All mimsy were the borogoves,
And the mome raths outgrabe.

We remember with gratitude his verses on the walrus and the carpenter, and from the wealth of what he has given us we may quote:

He thought he saw an Elephant,
That practised on a fife:
He looked again, and found it was
A letter from his wife.
"At length I realise", he said,
"The bitterness of life!"

Again, though there are many nonsense books and each reader will at once recall his own favourites, one more must be mentioned: "1066 and All That." This wholly admirable piece of fooling should be read aloud to any group of persons who take themselves too seriously and need a dose of laughter. It will be remembered that in the "Compulsory Preface" the authors write: "Histories have previously been written with the object of exalting their authors. The object of this History is to console the reader. *No other history does this.*" They express thanks to "their wife, for not preparing the index wrong", and add: "There is no index."

If we wish to look at nonsense from the point of view of quality or degree, we may imagine a base line (it had better be broad) representing the average man, if there is such a person—for our present purposes we shall presume that there is. Below the line will be placed the nonsense of persons of inferior intelligence, ending with that of the complete moron who provokes not laughter, but pity. On the base line or perhaps a little above it a place will be found for most of us and for those of our acquaintance more talented in nonsense-making. A high place will be found for those of the Lewis Carroll breed, for historians who "console" us and for similar folk. And here perhaps reference should be made to the paradox, a statement which does not make sense but which may have a deep philosophical significance: "Whosoever shall lose his life shall preserve it", and so on. A distinction should be made between nonsense and wit. Wit adds spice to social intercourse; it has been described as the salt of conversation, not the food. Wit is coveted by those who have it not; it is admired, but it is often feared. It is feared because it may have the pointed barb of malice. The witty man should cultivate tolerance; it is easy by a display of wit to score off another and even to be hurtful. To be the target of barbed wit is to be in difficulty. The "soft answer" turneth not away wit; rather does it seem to add a sting to its further display. Most people, lacking skill in repartee or the mastery of epigrams of an Oscar Wilde, take refuge in silence, and allow the witty one to be rude with impunity. It is no wonder that in the long

run the latter ends by loving himself. For all this, we could not be without the spice of our social intercourse, the salt of our conversation. We may conclude that while wit may give us pleasure and make us smile, nonsense in its right place brings laughter. Wit and nonsense may be combined and give much pleasure. About eighteen years ago a medical writer who had a ready wit, a sense of the ridiculous and a facile pen was invited, or perhaps we should say "dared", to write a skit on the "Current Comment" in this journal to which he was a regular contributor. His skit was published in the issue of April 17, 1937. Those who read it were delighted, and for the sake of those who have never seen it we reproduce it in the hope that they, too, will enjoy it:

> In these days of technical medicine it is probably true, even if regrettable, that more interest is taken in advances of a partly technical kind than in those concerned with the fundamental mechanism of the body. We are, as Lord Dawson recently said, "gadget-minded". This mild reproof need not concern us when we come to work of outstanding merit and value, such as that published in a recent issue of *The Journal of Cynical Medicine* on an apparatus for spraying the nasal passages of mice. No doubt many readers of these pages must have wished that some simple appliance was readily available for the purpose. Readers will recollect the extraordinary epidemic of a severe fungus infection of the scalp which spread over the rural districts of the eastern part of Australia during the war years. This was due to a remarkable plague of field mice, which invaded towns and dwellings alike, respecting neither the belongings nor persons of the people. Numbers of children were bitten during sleep; in one case it actually happened that the ear of a bank manager was bitten; this must be very rare. In another case it was reported that the ear of a bookmaker was also bitten, but this is almost certainly incorrect. However, a great need was felt at the time for reliable means of trapping the mice, which did not seem to be attracted readily by the usual sapid baits. Had some means existed at the time for spraying their nasal passages so as to remove any congestion or relieve local inflammation, no doubt the increase in acuity of the olfactory sense would have resulted in a much larger harvest in the mouse traps. The device seems to be very simple: manual control of the mouse has been eliminated, so long a trouble in laboratories with female technicians, though a certain periodicity in this variety of mouse-shyness has been noted from year to year, no doubt associated with fluctuations of fashions. The author is perhaps not quite exact in his methods, as he does not seem to have provided for spraying of each nostril singly, nor is there any allowance for deviation of the nasal septum or hypertrophy of the turbinates. This, however, is a detail, and probably only concerns the rhinologist with a "society" practice, where he may be unable, for motives of expediency, to refuse attendance on white mice belonging to the cadets of noble and/or wealthy houses.
>
> Further extension of this interesting work is to be expected, since it was discovered last year that an endemic granuloma in the ethmoid sinus of the dog flea was common in large cities. This gives rise to repeated sneezing on the part of the insect, which is not only a great source of annoyance to the smaller type of long-haired dogs, but is responsible for the setting free of small particles of dog hair through scratching. To this is due the greater incidence of asthma in some modern flats, and the clinician, being naturally interested in prophylaxis, would welcome the elaboration of a nasal spray suitable for the dog flea. This would prevent these troublesome attacks and no doubt save him (the clinician) much valuable time which could be better spent, for if a busy doctor must spend his scanty leisure in opening bottles, these need not always contain adrenaline.

Reference has been made to those who need a dose of laughter, and nonsense has been prescribed for them and indeed for all of us. In an essay on laughter published in these columns many years ago a quotation was made which justified this prescription. Lawrence Sterne made Tristram Shandy say in 1759 that he wrote his "Life and Opinions" ". . . against the spleen! in order, by a more frequent and a more convulsive elevation and depression of the diaphragm, and the succussations of the intercostal and abdominal muscles in laughter, to drive the *gall* and *bitter juices* from the gall-bladder, liver, and sweetbread of his majesty's subjects, with all the inimicitious passions which belong to them, down into their duodenums". We should all surely be the better for this.

Current Comment.

SAFETY PRECAUTIONS DURING EXPERIMENTAL ATOMIC EXPLOSIONS.

THE details of the safety precautions that are taken in Nevada, United States of America, during and after experimental atomic explosions are of interest to us, even though the testing site in Australia is much further removed from centres of population than is the Nevada one. Gordon M. Dunning[1] has given a survey of the Nevada procedure. Major consideration is given to meteorological conditions, with a weather station at the site in constant touch with the full Weather Bureau network, including six special stations ringing the site. An explosion can be cancelled up to a few seconds before the scheduled time if any adverse conditions arise.

Local precautions include the exclusion of the public from a wide area around the site, with aerial and surface surveys to ensure that no persons or animals have wandered into the area; local warnings of impending explosion times are issued; road blocks are placed on roads within sight or hearing of the site, and all vehicles are halted thirty minutes before firing time. Aircraft are not permitted to travel within 65 miles of the site for thirty minutes before and after the explosion.

The first main risk is from the intense flash of light. People around are warned not to look for the fireball, even from a distance, and especially through binoculars. Possible injuries are of the same nature as eclipse blindness, and since most explosions are timed for the pre-dawn period, for technical reasons, eyes are then in a most receptive condition. All workers at the site must wear special high-density glasses, or face away from the fireball. So far, there have been no known instances of eye damage off the site and only four on it.

All workers at the site are stationed in blast-proof shelters. Off the site, the only shock waves that matter are those reflected from the ozonosphere (an atmospheric layer 20 to 35 miles up) and those propagated through the troposphere (up to six miles high). Reflected shock waves may be heard as far as 150 miles from the site, but do not, as far as is known, cause any blast damage. The propagated waves may cause minor damage off the site; their strength depends on wind, humidity, temperature and similar conditions, and effects vary in different directions. It is usual, before each explosion, to fire off a high explosive charge to test blast wave propagation, and to warn people who might receive a blast wave to leave their windows open. So far there have been property damage claims totalling some £15,500, and no personal injury claims.

The major risks are from radioactive fall-out. Explosions high in the air result in the production of fine radioactive particles which nearly all go up into the stratosphere, whence they descend rather slowly; during this time most of their radioactivity decays, and the final result is a small fall-out of particles with low activity at the surface of the earth. Explosions on the ground result in the production of millions of tons of heavier radioactive particles which fall out mostly in nearby areas, and cause a high

[1] *J.A.M.A.*, July 16, 1955.

degree of contamination. One way to avoid this has been to explode the bombs on a high tower, with the adjacent ground sealed with asphalt. Outside the area, sections where the radioactive cloud is likely to be carried are closed to aircraft; clouds in these sections are monitored by aircraft. Preparations are made to evacuate threatened sections of the population if necessary, or to have them remain indoors to avoid β burns of the skin, and to decontaminate water, foodstuffs and buildings. It was found, however, that no β burns were recorded for human beings, though some cattle and horses within 20 miles of the site were burned, while nowhere did γ radiation reach a serious level.

In Australia similar precautions are taken, of a less elaborate nature naturally, since the site is so far removed from big centres of population, and there is no likelihood that the results of atomic explosions here would be any more dangerous than were those in Nevada.

FURTHER OBSERVATIONS ON CHILDREN AND THE CINEMA.

ON several occasions in past years attention has been drawn to the importance of the cinema in present-day life, and that hardy perennial, the cinema as a contributing factor in juvenile delinquency, has come up for discussion. No finality has ever been reached on the subject, although the impression remains that the cinema cannot be entirely absolved from blame. The most recent leading article in this journal on "Children and the Cinema" was published in the issue of August 5, 1950; it was based on the "Report of the Departmental Committee on Children and the Cinema; Presented to Parliament by the Secretary of State for the Home Department, the Secretary of State for Scotland and the Minister of Education by command of His Majesty, May, 1950". It is suggested that those interested could with advantage read this leading article again, since it is entirely relevant to the work about to be discussed. G. Heuyer, S. Lebovici, L. Bertagna and Madame Rebeillard[1] have for some years been engaged in an investigation of the immediately revealed influence of films on children aged ten years and over. These authors employ the term "filmology", which they define as a multidisciplinary science dealing with the physiological, psychological, sociological and pathological reactions of the person watching a film. They state that the film has a social role, and in this regard its effect is complex. First, its role is one of instruction and culture; the educational film requires the spectator to have a high enough level of intelligence to understand it. Second, the role of the film is one of entertainment, relaxation, compensation and escape. The third role is that of intentional or unintentional propaganda. Heuyer and his co-workers, six years ago, determined to make use of the clinical material available at the psychiatric clinic for children where they work. They argued that, although it is possible to study successfully the physiological and psychological reactions of normal children and adolescents, in the field of apperception and comprehension the study of affective reactions in normal children gives more debatable results. The normal child or adolescent is easily able to control his affective reactions, to discuss and to argue. At the clinic they investigated the reactions of maladjusted children—children and adolescents with affective disturbances which had brought about behaviour disorders (always, the authors state, stemming from the child's emotivity and anxiety) in relation to the family, to the school, to the workshops where they were apprenticed, and in general to the child's social group. The children were in no way mentally affected, and were able to follow a film and even to enjoy it. However, such children in comparison to normal children have more intense reactions which are easier to observe. Those forming the subjects of the investigation were first tested to make sure that they were capable of following the films shown.

There is no need to describe in detail the way in which the observations were made, but the findings are of interest in any country. It was found that the child with a mental age of less than seven years sees the pictures on the screen and can follow short sequences, but does not understand their significance. When the child has a mental age of less than nine or ten years, he can follow a sequence of pictures, but does not understand their meaning. Thus, a child aged under about ten years cannot be influenced by a film, because he cannot understand the meaning of the succession of sequences. The effect of a film on children over this age can be immediately detected in the fields of apperception, comprehension and affection. The comprehension of a film requires two things—the ability to follow the succession of sequences, for which a mental age of ten years is necessary, and the ability to grasp the meaning of the film as a whole, for which the child must have a mental age of at least twelve years. With regard to comic films, only if they are simple are they within the understanding of those with a mental age of less than twelve years; Charlie Chaplin is not for children. An interesting observation is that present-day cartoons require a mental age of at least twelve years; such films are not often understood by children below this mental age, because the animated drawings are so stylized and distorted that identification becomes difficult. Heuyer and his co-workers find that the children's affective reactions to the films provide valuable data for the study of individual tendencies. Films can serve as projective tests, either by detecting tendencies in the child's character, or by presenting situations which coincide with a personal conflict. The mechanism of the affective reactions is essentially that of projection and identification. Although children and adolescents react individually to films, the differences in reaction between the sexes have important consequences. The part played by the cinema in inducing delinquent tendencies is by no means clear; but "gangster" films have an effect by teaching techniques of delinquency and crime. Films have an effect on the child's mental content and his social behaviour; thus they influence the adolescent's way of life. Hueyer and his associates recommend electroencephalographic and biological investigations, to provide a physiological and scientific foundation for the psychological observations on affective reactions.

One or two interesting sidelights on the children are also recorded. It appears that they enjoyed their roles as critics, particularly those with paranoic tendencies, who came down heavily on every defect, even the smallest. Moreover, whatever their basic abnormalities, in general the children expressed great disapproval of wrong behaviour on the part of the characters in the films, especially when it was of the same type as their own behaviour disorders. This attitude is by no means confined to maladjusted children attending a psychiatric clinic; in an inverted form it echoes the words of Saint Paul: "For the good that I would I do not; but the evil which I would not, that I do."

[1] *Presse méd.*, July 16, 1955.

SERUM GLUTAMIC OXALACETIC TRANSAMINASE IN ACUTE MYOCARDIAL INFARCTION.

LIVING CELLS contain a great variety of enzyme systems, many of which can be estimated quantitatively, with some accuracy, by comparatively simple means. It was inevitable that someone would endeavour to use the amount of leakage into the blood of specific enzymes from damaged cells within the body as a measure of cell destruction in particular organs. This has now been done by J. S. La Due and F. Wróblewski,[1] who have used the increase of the enzyme glutamic oxalacetic transaminase as a measure of the presence of and extent of acute myocardial infarction. This enzyme is probably present in all cells; it, at least, has a very wide distribution. It is the enzyme necessary for the reversible transfer of the α amino nitrogen of aspartic acid to α ketoglutaric acid with the formation of

[1] *Circulation*, June, 1955.

glutamic and oxalacetic acid. Heart muscle shows the greatest activity of any animal tissue examined, followed by skeletal muscle, liver and kidney. Normally serum contains 10 to 40 arbitrary units per millilitre and levels above this were not seen in patients with infectious, neoplastic, metabolic or degenerative diseases in which acute destruction of heart, skeletal muscle or liver tissue could be excluded. Serum from dogs in whom myocardial infarcts had been induced showed serum figures raised in amounts roughly proportional to the size of the infarction. When an animal dies from any cause the serum glutamic oxalacetic transaminase activity increases very greatly in amounts proportional to the time since death. The sera of 50 patients with unequivocal transmural myocardial infarctions were analysed for the transaminase activity at varying times after the onset of chest pain, and transaminase elevations of from 70 to 600 units within 12 hours to six days after injury were found in every patient. Another 25 patients examined in less detail showed similar rises. Typically there is a rise to 500 units or more during the first twelve hours with a gradual return to normal values by the sixth day. There seems to be a rough correlation between the height of the maximum serum transaminase activity and the size of the myocardial infarct as indicated by electrocardiographic examination. Serum glutamic oxalacetic transaminase is unaffected by *angina pectoris*, coronary insufficiency, heart failure or digitalis in the absence of active heart cell damage. In fifteen cases of *angina pectoris* or coronary insufficiency with nonspecific electrocardiographic changes there was elevated enzymatic activity of their serum, presumably evidence of heart muscle damage. Elevated serum transaminase activity has been found following acute liver damage, skeletal muscle damage, myositis and arterial occlusion, but in none of these does one get the curve of increase and decrease seen in acute myocardial infarction. Not enough has been done yet to enable one to estimate the clinical value of the test, but it is very promising. The authors state that the enzyme is stable in serum for several days at 0° to 5° C. The method of analysis is not given, but it is said to require only five minutes per determination. It would seem that the test depends on the interaction between oxalacetic acid formed and D.P.N.H. in the presence of malic dehydrogenase with the formation of malic acid and D.P.N. and the determination of the D.P.N. spectrophotometrically.

DETERMINATION OF RHEUMATIC FEVER ACTIVITY.

IN the early stages of the disease it is not always easy or possible to distinguish rheumatic fever from other diseases with similar clinical manifestations. A test which would help in making the diagnosis and in ascertaining the degree of activity of the rheumatic fever process would be useful. The principle of antigen-antibody reaction has often been used in various ways to identify infections diseases. R. K. Skillman, W. Spurrier, I. A. Friedman and S. O. Schwartz[1] have devised two tests, based on this principle, for the recognition of rheumatic fever and its degree of activity. Erythrocytes, which have been coated with an antigen, are agglutinated when antiserum prepared from this coating antigen is added. When complement is added to this system, under certain conditions, hæmolysis occurs.

Rheumatic fever is associated with tissue reaction to group A β hæmolytic streptococci, so heat-killed streptococci of this type, isolated from patients with rheumatic fever, were used as antigen. Two methods were employed. In the first the serum of the patient was used as a source of antibody; as the source of antigen red corpuscles coated with heat-killed group A β hæmolytic streptococci were used. Complement was added to produce hæmolysis. In the second method antiserum was obtained from rabbits injected with β streptococci. For the antigen the red corpuscles from the patient were coated with β streptococci and the test was carried out as an agglutination test. The first method was somewhat the more sensitive. For the antigen group A β hæmolytic streptococci isolated from patients with rheumatic fever and belonging to types 5, 6, 12 and 19 were used either separately or all four pooled. The pooled antigen gave the most sensitive and consistent results.

The 165 determinations on 78 patients with rheumatic fever at various stages correlated with the clinical condition of the patient at the time of the test. The hæmolysis method showed that 98% of those assessed as active gave a positive reaction; of those considered stable 73% gave a positive reaction, and of those considered inactive 48% gave a positive reaction. As the disease progressed towards inactivity the titres became lower and gradually became negative at the same time as the disease became inactive. The height of the titre during the active stage of the disease was not necessarily indicative of the severity of the disease. As controls 77 patients with a variety of diseases were used, from whom, in 13 cases, β streptococci were grown in culture. In no case among the controls was a positive reaction given.

[1] *Arch. Int. Med.*, July, 1955.

INJURIES TO THE CHEST.

FRACTURE of one or more ribs is a relatively common injury which is usually taken fairly lightly. However, R. L. Rapport, R. B. Allen and G. J. Curry[1] have analysed figures from the Hurley Hospital (Michigan, United States of America) and have concluded that by reason of complications and a surprisingly high mortality rate, the subject of fractured ribs merits serious consideration. These writers found that during the six years from 1947 till 1952, more than 5% of patients admitted to the section for surgery of trauma had broken ribs; during this time, 490 in-patients and 240 out-patients were treated for fractured ribs. Exclusive of other injuries, the complications among the 490 in-patients which were due solely to fracture of one or more ribs were: subcutaneous emphysema, 67; multiple fractures ("stove-in" chest) with paradoxical respiration, 21; hæmothorax, 62; pneumothorax, 59; pleural effusion, 9; contused lung, 62; "traumatic wet lung" (retained secretions leading to tracheobronchitis, atelectasis, and even pneumonia), 96; mediastinal complications, 8, associated abdominal complications, 58. Deaths numbered 12 due to thoracic injury, 10 due to associated injury, and 12 due to both; it was concluded that deaths in which thoracic injury was the sole or a decisively contributing factor represented 4·9% of the 490 in-patients.

These are rather formidable figures, even when the 240 out-patients with, presumably, uncomplicated fractures are included, for the deaths even then represent 3·3%. Rapport and his colleagues emphasize "traumatic wet lung", pneumothorax and hæmothorax as the commonest and most important complications, and stress the need for prompt and vigorous treatment. For hæmothorax, early and complete aspiration without air replacement, repeated often, is recommended as the correct procedure; if hæmorrhage nevertheless continues, early thoracotomy with evacuation of clots and hæmostasis is advised. For a small, closed pneumothorax (less than 25%) no specific treatment is required. If collapse is greater than 25%, closed catheter drainage is recommended; tension pneumothorax constitutes a surgical emergency requiring immediate aspiration, and possibly early thoracotomy.

For the sequence of contused lung, retained secretions, tracheobronchitis and atelectasis, which has been labelled "traumatic wet lung", these workers demand first an unobstructed airway and evacuation of the bronchial tree. They condemn adhesive strapping and opiates out of hand—these do much harm and little good. Intercostal nerve block, performed as early as possible, relieves pain and enables the patient to cough freely and clear his own secretions. If coughing is impossible or ineffective, nasotracheal catheter aspiration, bronchoscopy, and even tracheotomy may be necessary.

[1] *Arch. Surg.*, July, 1955.

The above figures for "stove-in" chest with paradoxical respiration (21 among 730) cannot, unfortunately, be directly compared with some others from the Birmingham Accident Hospital (England), but it would appear that at Hurley this condition represented 21 of 9800 total accident cases, while at Birmingham it occurred only eight times among 344,000 injured persons. H. Proctor and P. S. London[1] state that the anterior type of "stove-in" chest is commonly due to the impact of the steering wheel of an automobile, while the lateral and posterior types are due to running-over or crushing accidents. Proctor and London recommend stabilization with sandbags or by posture; they are not in favour of adhesive strapping; they mention intercostal nerve blocking, but prefer procaine given intravenously. Once shock has been treated, the floating segment of chest wall is fixed, preferably by traction by wires and hooks to a special cage.

In this connexion, an interesting case has recently been reported by F. H. Ellis, H. A. Andersen and A. B. Hayles.[2] A three-year-old girl, over whose chest the front wheel of an automobile has passed, had no fractures of her ribs, but had massive positive pneumothorax with complete collapse of the lung. Two pumps were needed to aspirate the air at first, and even after air leakage had ceased and closed catheter drainage had been instituted, there was no expansion of the lung. Thoracotomy a week later revealed a complete rupture of the right upper-lobe bronchus. Repair of the bronchus was followed by a good recovery. Here again is emphasized the need for prompt aspiration when a massive positive pneumothorax occurs. Failure of further conservative treatment was inevitable, of course, because of the gross injury to the bronchus. The authors suggest that earlier thoracotomy is desirable under such circumstances.

Possibly it would be an over-statement to class such cases as "broken ribs", since in practice the simple fracture of a rib can usually be distinguished with ease from a crushing of the chest with complications. However, Rapport and his colleagues have produced a report that is of considerable interest and value.

FUNGOUS INFECTIONS OF THE FEET.

Two opposing views regarding the epidemiology of tinea infections of the feet have recently appeared. In the *British Journal of Dermatology*, July, 1955, R. H. Broughton discusses reinfection from socks and shoes; he accepts, uncritically, the proposition that primary infection is easily acquired by contagion in washing places and close living quarters, and then states that reinfection is due to the establishment of a permanent reservoir of infection provided by the retention of fungus-laden epidermal scales in the meshes of woollen and cotton socks. Broughton's experiments showed that after socks were worn for two days, dyed epithelial squames could survive at least six launderings, and that *Trichophyton interdigitale* could survive for five months in a sock stored under moist conditions; moreover, he succeeded in growing cultures of *T. interdigitale* from the socks of 35 of 104 patients with tinea of the feet, of six of 19 patients with suspected infection, and of five of 100 apparently uninfected controls. He also showed that hot conditions, and the heat and moisture of thick woollen socks, were conditions favourable to the development of tineal infections of the feet. Accordingly, Broughton suggests that a broad-meshed nylon sock would be cooler and also less likely to provide harbourage for infected epithelial squames.

Here might be interpolated the observations of F. H. Packer,[3] who investigated 22 patients suffering from excessive sweating of the feet. Only one was a woman, and she suffered only when wearing woollen socks. All the men habitually wore woollen socks. After wearing thin cotton socks inside their woollen ones for two weeks, 16 had no excessive sweating, two were improved, two showed no improvement, and two were lost sight of. Packer concluded that a specific sensitization to wool in some people was the factor causing excessive sweating, rather than just the heat of woollen socks.

R. L. Baer, S. A. Rosenthal, H. Rogachefsky and J. Z. Litt[1] also discuss the source of infection in *tinea pedis*. They state that the usually accepted source of infection is carpets, bath mats and the floors of swimming pools and shower rooms, but that there is a dearth of experimental evidence that fungi can be cultivated from these sources. They also state that although fungus can be cultivated from the footwear of patients suffering from tinea, it can equally readily be cultivated from the footwear of those who have no clinical evidence of infection, and that there exists no proof that footwear is a source of infection or reinfection. These workers accept the fact that infection can be caused by placing cultivated fungus between the toes after the skin has been macerated for some time, or by holding the fungus in contact with skin which is kept moist with adhesive tape bindings, but claim that these are artificial and unnatural conditions which prove nothing.

Baer and his colleagues showed that when patients with tinea soaked their feet for fifteen minutes in water, in 54 of 78 instances fungous elements were found in the water; moreover, of 28 subjects clinically free of tinea, four also produced fungous elements after soaking their feet in this way. Thereafter 14 clinically and microscopically uninfected patients soaked one foot in water containing this fungous material, and 21 in water contaminated by cultivated fungus. None developed clinical signs of tineal infection, although in 27 fungal elements were subsequently found in scrapings from the exposed foot, and in 15, from the control foot. Baer and his colleagues accordingly conclude that exogenous contagion is not the pathway of infection, but that lowering of resistance allows fungal elements already living saprophytically in the skin to set up invasive lesions. They recommend, among other measures, the wearing of perforated shoes in hot weather to reduce heat, allow of evaporation and minimize maceration, and the wearing of woollen socks in preference to nylon, to increase absorption of sweat and so minimize maceration.

None of these people has completely proved his case, but each offers some useful evidence. Packer has shown that it is not the heat of wool which causes excessive sweating, but some irritating property of woollen socks; this is not necessarily a specific sensitivity to wool. Packer failed to take dyes into consideration; but he has shown that some people react by excessive sweating to some woollen socks, or alternatively that some woollen socks cause some people to react by sweating excessively. Such people suffer the necessary degree of maceration of the skin of their feet to favour the growth of tinea. If, as Broughton considers, it is quite easy to acquire infection in shower rooms, why does he insist that infected footwear is the true source of reinfection, especially as he offers no proof that the wearing of infected socks does in fact cause infection? He misses the point that if shed epithelial scales carry viable fungal elements even in the absence of clinical lesions, then the about-to-be-shed scales must also carry them. Baer and his colleagues are almost certainly correct in stating that fungi may grow saprophytically in normal skin, and that for various reasons they can become invasive and cause clinical lesions, but this does not support their argument that exogenous infection does not occur naturally. They are quite inconsistent—they deny that infections following artificial maceration of the skin of the feet prove anything, yet include the wearing of ventilated footwear and absorbent socks, to prevent maceration, in their prophylactic measures; they regard the failure of infection to develop after soaking the feet in water containing small amounts of fungus as proof that exogenous infection does not occur, yet they neglect the possibility that the abrasive effect of grains of sand, concrete, or even wooden floors, in removing infected epithelium from the feet of some people and grinding it deeply into the skin of others, may account for many primary infections.

[1] *Brit. J. Surg.*, May, 1955.
[2] *Proc. Staff Meet., Mayo Clin.*, June 29, 1955.
[3] *The Practitioner*, August, 1955.

[1] *Am. J. Pub. Health*, June, 1955.

Abstracts from Medical Literature.

PHYSIOLOGY.

Work Capacity After Blood Donation.

B. BALKE, G. P. GRILLO, E. B. KONECCI AND V. C. LUFT (*J. Appl. Physiol.*, November, 1954) report that work capacity was determined during exercise on the treadmill; heart rate, blood pressure and respiratory gas exchange in response to an increasing work load were used as criteria of performance. Experiments on the after-effects of blood donation (500 millilitres) were carried out on 14 subjects at different intervals after venesection. Within one hour after blood donation the reduction in optimal work capacity was statistically very significant as compared with repeated control tests made previously. Results obtained forty-eight and seventy-two hours after blood loss were not significantly different from the normal. Determinations on the eighth and tenth days after blood donation revealed an improvement in work capacity which was statistically significant.

The Mechanism of Reticulocytosis.

R. H. RIGDON, D. SMILEY, G. CRASS AND N. MARTIN (*Texas Rep. Biol. & Med.*, Spring, 1955) report that the young duck is an excellent experimental host for the study of reticulocytosis because of the rapidity of growth and the normal presence of large numbers of reticulocytes within the peripheral blood. Marked changes may be produced in the number of reticulocytes in the peripheral blood of the duck within seventy-two hours. Reticulocytes completely disappear from the peripheral blood within seventy-two hours after all foods are withdrawn from young ducks. These cells return to the peripheral blood within a similar period when food is replaced. Ducks fed only sucrose or vegetable fat (Wesson oil) show a rapid diminution in the number of reticulocytes in the peripheral blood. Ducks fed only casein do not show a corresponding diminution in the number of reticulocytes in the peripheral blood. The reticulocyte response to anoxia in the duck is much greater in the presence of an adequate diet than it is in ducks receiving no food. It is suggested from these experiments that anoxia is the basic stimulus for the production of reticulocytes. This stimulus may result either from a deficient amount of oxygen reaching the bone marrow or through some failure in function of an enzyme system within the bone marrow. It is suggested that cobalt may produce the latter effect.

Body Heat Production and Surface Temperatures in Response to a Cold Stimulus.

J. P. MEEHAN (*J. Appl. Physiol.*, March, 1955) reports that metabolic rates were simultaneously measured with multiple surface and deep body temperatures on an experimental group of Alaskan native subjects and on a control group of Caucasian military personnel during a standard exposure in a cold room. The initial or basal metabolic rates of all the subjects were found to be at normal accepted values. The native subjects did not have an elevated basal rate. On exposure to cold, the native subjects showed the greater increase in metabolic rate. This increase was due to greater shivering on the part of the natives. During the cold exposure, the native subjects kept their hands and feet warmer than the control subjects. Trunk skin temperatures and mean body temperatures for the two subject groups were not significantly different. The control group developed the greater total loss of body heat.

Motion Sickness.

G. H. CRAMPTON (*J. Appl. Physiol.*, March, 1955) reports that 22 men were stimulated in an elevator-like apparatus for one hour or until they vomited, whichever occurred first. Simultaneous measures of a number of physiological variables were obtained. The vomiting group could be distinguished from the non-sick group by the following differences: greater increase in pulse rate, greater vasoconstriction, greater increment in ventilation, more abrupt decrement in gastric tone, more sweating and more facial pallor. With the exception of pallor, these differences were evident only in the comparison of group means because of the great between—and within—subject variability. The only common sequence of events, true of most individuals, was the onset of pallor, then the report of nausea, and finally vomiting. All other variables showed considerable individual variation.

Individual Salivary Gland Secretion under Conditions of Reduced Exogenous Stimulation.

L. H. SCHNEYER AND L. K. LEVIN (*J. Appl. Physiol.*, March, 1955) report that the rate of secretion by the individual major salivary gland pairs was determined for 23 young male adults under conditions of reduced exogenous stimulation. Under these essentially "resting" conditions, it was found that the submaxillary glands contributed approximately 69%, the parotid glands 26% and the sublingual glands 5% (mean values) of the total secretion derived from these three major gland pairs.

Glycerol Pectate for Plasma Volume Replacement and Expansion.

S. W. HANDFORD, C. McC. SMYTHE, J. P. GILMORE, R. S. LEOPOLD, R. H. KATHAN AND H. G. ARM (*J. Appl. Physiol.*, March, 1955) report that intravenous and oral administration of a 4% solution of glycerol pectate, equivalent to 5% of body weight, has no significant effect on clotting and bleeding time. However, when mixed *in vitro* with human blood, it accelerates clotting time but causes no agglutination of erythrocytes that might interfere with cross-matching for purposes of transfusion. Symptomatically, no antigenic responses were observed following multiple infusions into dogs, rats, mice and rabbits over a period of fourteen days. There was no gross or microscopic evidence of pathological changes in the tissues and organs of animals following large single and multiple infusions of glycerol pectate that might contraindicate its use for plasma volume replacement and expansion. The growth-supporting potential of glycerol pectate and dextran (pH adjusted and unadjusted to near neutrality before use) tested on nine organisms has been determined. Bacteria survive in all the test substances except the unadjusted glycerol pectate; but when adjusted to neutrality, a 4% solution of this material provides suitable conditions for the survival of the test organisms. There is no difference in survival over a forty-eight hour period of the test fungi in adjusted and unadjusted solutions. Both directly and indirectly the pH of the solutions appears to be an important governing factor. It was noted that the pH of dextran ("Expandex", Commercial Solvents) and isotonic saline (Baxter's "Travenol" and United States Standard Products Company's isotonic solution of sodium chloride) issued for parenteral use was considerably lower than neutrality.

Pulmonary Ventilation During Exercise and Inhalation of Carbon Dioxide.

F. N. CRAIG (*J. Appl. Physiol.*, March, 1955) reports that respiratory minute volumes (V) of three men were followed during inhalation of carbon dioxide mixtures of up to 8% strength (C) and standing, walking or running on a level treadmill at speeds up to six miles per hour (M). The conditions were studied in combinations up to 6% of carbon dioxide and four miles per hour. The results were fitted by the equation $\text{Log } V = d + eC + dM - gCM$ with an average deviation of two litres per minute. In this system the lines representing constant carbon dioxide concentration or treadmill speed converge and when extrapolated come to a point. It is concluded that while the minute volume was multiplied by factors for carbon dioxide and treadmill speed, each factor operated so as to diminish the action of the other.

Heat and Excretion in Man.

G. S. KANTER (*J. Appl. Physiol.*, March, 1955) reports that exposure (four to six hours) to desert-like conditions (temperature 120° to 130° F., relative humidity 10% to 20%), with no water available, is tolerated by man without undue effects. One body defence against the imposed heat stress involves sweating to aid the regulation of body temperature by evaporative cooling. The rapid dehydration can be measured by the weight loss (which is mainly water loss) and is manifested by the eventual feeling of fatigue and increased heart rate. Urine flow is greatly reduced, probably owing to the action of the posterior pituitary lobe during the progressing dehydration as well as to an alteration in the renal dynamics involving a fall in glomerular filtration rate during heat stress. The excretion of sodium and chlorine is depressed by heat, while the excretion of potassium tends to increase. Bicarbonate disappears from the urine after one to two hours, during which time an acidosis

sets in. The urine pH falls steadily throughout the exposure, while the excretion of phosphate (monobasic) simultaneously increases. Examination of the arterial pH revealed that a true acidosis did exist. That it was not respiratory in origin is based on the finding of a fall in carbon dioxide content indicating a mild hyperventilation. The acidosis is therefore assumed to be metabolic in nature. The mechanism of the acidosis awaits further investigation.

Protective Effect of Carbon-Free Fraction of India Ink Against Snake Venom.

S. GARB, A. SCRIABINE, B. B. ROY, V. VENTURI AND M. PENNA (*J. Lab. & Clin. Med.*, April, 1955) report that in a series of experiments on rats and mice it was found that some as yet unidentified substance in the carbon-free fraction of Higgins India ink afforded a significant degree of protection against the lethal effects of both rattlesnake and cobra venoms when injected subcutaneously into the same animals as the constituents of India ink did not protect. A number of known constituents of India ink were tested and also found to be ineffective. Some of the implications of these findings are discussed.

BIOCHEMISTRY.

Thyroxine.

J. A. TABACHRICK AND D. BONNYCASTLE (*J. Biol. Chem.*, April, 1954) have determined the coenzyme A (a compound of pantothenic acid) levels of liver, heart, brain and small intestine in rats which were normal, thyroidectomized, or thyroidectomized and treated with 150 γ of sodium L-thyroxine pentahydrate. The level of coenzyme A in these tissues was greatly influenced by thyroxine.

Hyaluronic Acid.

W. P. DEISS AND A. S. LEON (*J. Biol. Chem.*, January, 1954) have isolated an acid mucopolysaccharide from a dilute alkaline extract of fresh bovine heart valves. It is unlike those previously isolated from this tissue and consists of equimolar quantities of hexosamine, hexuronic acid, acetyl and sulphate. Tentative classification of this heart valve mucopolysaccharide as a sulphate ester of hyaluronic acid, apparently identical with corneal hyaluronosulphate, is based on its optical rotation and its enzymatic hydrolysis by both testicular and pneumococcal hyaluronidases.

Glycogen.

M. R. STETTEN AND D. STETTEN (*J. Biol. Chem.*, March, 1954) have injected radioactive glucose intraperitoneally into rats and after various time intervals isolated glycogen from liver and from carcass. Each glycogen sample was exhaustively digested with β-amylase and the distribution of C^{14} between the maltose (periphery) and the limit dextrin obtained was determined. In the glycogen from liver the peripheral tier initially accounted for the bulk of the C^{14}. With the passage of time an increasing fraction of the labelled glucose was found in the limit dextrin and by the twelfth hour this fraction exceeded that in the periphery. A contrasting situation was encountered in the glycogen of the carcass wherein, even after forty-eight hours, the major fraction of the labelled glucose was found in the peripheral tier. Three hours after injection of glucose-C^{14} into a fasted rat, radioactivity was found to be nearly evenly distributed between the periphery and the limit dextrin of liver glycogen, whereas the distribution in carcass glycogen was little influenced by previous fasting. These findings show that glycogen, although yielding only glucose upon total hydrolysis, is metabolically inhomogeneous. Glycogen turnover *in vivo* is not merely a replacement of pre-existing molecules by newly formed glycogen molecules. Glucose residues situated peripherally in the glycogen molecule are renewed faster than those more centrally located, and this contrast is more striking in muscle than in liver.

Wound Regeneration.

M. B. WILLIAMSON AND H. J. FROMM (*J. Biol. Chem.*, February, 1955) have studied the early stage of wound tissue regeneration in rats. They report that the methionine content of wound proteins is greater than the cystine content. Later the content of cystine becomes very much higher than that of methionine. This has been taken to mean that two different types of proteins are synthesized by the regenerating wound tissue. By use of S^{35}-labelled methionine and cystine, it has been shown that sulphur metabolism is stimulated during wound tissue regeneration and that the liver methionine supplies a large part of the cystine required by the regenerating wound tissue.

Fatty Acids.

A. ALLEN *et alii* (*J. Biol. Chem.*, February, 1955) have studied the effect of glucose on fatty acid oxidation. Various tissues of the rat in the form of slices or whole homogenates were allowed to oxidize added C^{14}-labelled fatty acids, both in the absence and in the presence of non-labelled glucose, and the degree of substrate oxidation was measured by the incorporation of C^{14} in respiratory carbon dioxide. Under no circumstances did the presence of glucose lower the oxidation of the added fatty acids, even when its concentration was far higher than that of the fatty acid. The oxidation of endogenous palmitic acid of tissue lipides was likewise little affected by the presence of glucose. The data are taken to indicate that there is a basal fatty acid catabolism occurring generally in tissues, which is not suppressed by the abundant presence of carbohydrate.

Muscular Dystrophy.

K. E. HURLEY AND R. J. WILLIAMS (*Arch. Biochem.*, February, 1955) have studied urinary levels of creatinine, phosphate, glycine, alanine, serine, threonine, valine, leucine, taurine, citrulline and arginine in a group of young males with muscular dystrophy and a group of young normal males. Threonine, valine, leucine, arginine and taurine levels in urine have been found to be higher in the subjects of muscular dystrophy. Creatinine and phosphate have been found to be excreted in smaller quantities in subjects of muscular dystrophy. Intra-individual and inter-individual differences seem to occur in the excretion of all substances studied. The intra-individual variations are almost never as wide as the inter-individual variations. It is proposed that a dietary supplement containing vitamins *E* and B_{12} and folic acid, the sulphur amino-acids, arginine and glycine, with or without other factors, be tested for its efficacy in alleviating the metabolic difficulties in cases of muscular dystrophy.

Urine.

R. G. WESTALL (*Biochem. J.*, June, 1955) has studied the aminoacids and other ampholytes in 100 litres of urine from a normal adult male subject by using ion exchange fractionation and chromatographic procedures. Of the ninhydrin-reacting substances 27 could be identified by paper chromatography. A further 38 substances, five of which appeared after hydrolysis, gave spots not corresponding to known substances. These have been plotted on a chromatographic map. Ten of the unknowns are stable to the conditions of acid hydrolysis. The remaining 28 substances are unstable to hydrolysis, mostly yielding varying numbers of the common aminoacids.

Cobalamin.

I. CHANG AND B. C. JOHNSON (*Arch. Biochem.*, March, 1955) have studied the effect of vitamin B_{12} deficiency on the conversion of α-C^{14}-labelled glycine to serine and choline in baby pigs fed on α-protein vitamin B_{12}-deficient synthetic milk ration containing 2·2% of glycine, 0·8% of methionine and 0·1% of amino-ethanol. Glycine-α-C^{14} was shown to be a precursor of serine and of both the amino-ethanol and the methyl moieties of the choline molecule in the pig as in the rat. The addition of vitamin B_{12} to the diet caused a five-fold increase in incorporation of the α-carbon of glycine into the methyl group of choline, while vitamin B_{12} feeding had no effect on the incorporation of the α-carbon of glycine into serine and aminoethanol.

Phosphatases.

R. WAGNER AND A. YOURKE (*Arch. Biochem.*, January, 1955) have studied phosphatase activity in leucocytes and blood platelets of horse blood for different substrates and at different values of pH. Linear relation between the number of leucocytes and their phosphatase activity is detectable only within a limited enzyme concentration for a given concentration of the substrate. Dialysis against distilled water, freezing and thawing, and homogenizing enhance the yield of inorganic phosphorus liberated. Freezing of the undialysed cell suspensions preserves the enzyme for a considerable length of time. Glucose-6-phosphatase and β-glycerophosphatase in leucocytes are alkaline phosphatases. Blood platelets carry an acid phosphatase. The peak of β-glycerophosphatase activity in horse blood leucocytes at pH 5·0 is an artifact, produced by the blood platelets.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at the Alfred Hospital, Melbourne, on May 4, 1955. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical staffs of the hospital.

Hypotensive Drugs and Parenchymatous Nephritis.

DR. J. ERIC CLARKE showed two patients to raise discussion on the use of "hypotensive" drugs in certain cases of parenchymatous nephritis.

The first was a girl, aged seventeen years, who had been admitted to hospital on March 7, 1955, suffering from acute nephritis and acutely distressed with cardiac failure. Her blood pressure on admission was 170 millimetres of mercury, systolic, and 130 millimetres, diastolic. An X-ray examination of the chest showed gross bilateral changes of fan-shaped distribution—the typical "uræmic lung". Dr. Clarke said that if the hypertension was regarded as the important factor in precipitating cardiac failure, it would be tempting to use one of the hypotensive drugs. He discussed the nature of the cardiac failure and lung changes, and gave reasons for not using those drugs. He said that as it turned out, there was gross oliguria and a grossly elevated blood urea level (230 milligrammes per 100 millilitres), and management for the first ten days was chiefly directed to controlling the electrolyte and fluid balance. At the time of the meeting she was well, but had some albuminuria, and her blood pressure was 140 millimetres of mercury, systolic, and 90 millimetres, diastolic. Her heart was of normal size, her lung fields were clear, and her blood urea content was 35 milligrammes per 100 millilitres.

The second patient was a man, aged forty years, who in November, 1954, following a sore throat ten days earlier, had developed acute nephritis. The albuminuria and œdema had persisted with a fall in the serum protein levels and a rise in the blood cholesterol level, so that he presented the typical picture of "subacute nephritis" or "type 2 nephritis". A week before the meeting he was admitted to hospital with hypertensive encephalopathy; papilloedema, hæmorrhages and exudates in his ocular fundi; and a blood urea content of 50 milligrammes per 100 millilitres. It was suggested that although the case was one of progressive nephritis, the immediate threat was from the malignant hypertensive phase, and that amelioration of the condition might be possible with the careful use of hypotensive drugs—it was proposed to use "Ansolysen".

Rheumatic Carditis.

DR. H. B. KAY showed patients illustrating the various phases of rheumatic carditis and discussed aspects of management in the prevention of recurrences—namely, the use of maintenance therapy with sulphonamides and salicylates, and of penicillin during acute streptococcal infections. In the drug therapy of acute rheumatic fever, it was recommended that full doses of salicylates be used as a routine; if response was inadequate, then the use of cortisone was recommended, and if control was still not achieved, then the use of ACTH.

The first patient was a girl, aged fourteen years, who had suffered a recurrence of rheumatic fever in October, 1953, with evidence of mitral incompetence. Despite hospital treatment until the present, her sleeping pulse rate, erythrocyte sedimentation rate and antistreptolysin titre had remained elevated. She had suffered no sore throats, and results of throat swab examinations were negative; tonsillectomy in November, 1954, was followed by further and persistent elevation of sedimentation rate (36 millimetres in one hour) and antistreptolysin titre (833 units). No other septic foci were detected, and it was not considered that tonsillectomy had proved of any value. She had now commenced maintenance treatment with sulphonamide and "Disprin"; if her condition remained active, it was considered that she should have cortisone therapy.

The second patient, a man, aged twenty-one years, had had rheumatic fever at the age of eight years and a recurrence at the age of eleven years. In 1949 he had had only a soft systolic murmur at the apex and in 1951 a late systolic murmur at the apex; now he had a presystolic murmur. An unusual feature was an episode of *erythema nodosum* in October, 1954. At that time the erythrocyte sedimentation rate was 16 millimetres in one hour and the antistreptolysin titre 250 units. His condition was at present quiescent, and he was on maintenance treatment with "Disprin" and sulphonamide. As a contrast was shown a male, aged sixteen years, with a history of rheumatic fever three years previously, but now showing typical joint changes of rheumatoid arthritis. On auscultation a grade II systolic murmur was audible at the apex, but X-ray appearances of his heart were normal. He was being observed from the point of view of possible "rheumatoid" heart disease.

The next patient was a girl, aged twenty-five years, who had a history of rheumatic fever at the age of seven years and eleven years, with consequent mitral valve involvement. In 1950 she had had subacute bacterial endocarditis due to *Streptococcus viridans*, with good recovery. In 1952 she had had a further episode of rheumatic fever with associated pericardial effusion. She failed to respond to full salicylate therapy, but responded well to cortisone, and was on maintenance cortisone therapy for eleven weeks with full recovery. In 1955 she had a normal delivery of a full-term child, without any cardiac complications. On X-ray examination her heart size was within normal limits with slight left auricular enlargement.

Two other patients were demonstrated, showing the favourable and unfavourable features in deciding to submit a patient with mitral stenosis to mitral valvotomy.

Clinical Phonocardiography.

DR. J. M. GARDINER outlined the use of the phonocardiogram in clinical diagnosis. He said that the instrument was designed to record heart sounds and murmurs in much the same way as they were registered by the ear in clinical auscultation. It had the advantage, however, that it incorporated reference tracings—electrocardiogram, carotid tracing or jugular phlebogram—and that records might be taken from different areas simultaneously, or at different frequencies. Hence it could define the exact time relationships of heart sounds and heart murmurs accurately, study the effect of respiration on them, delineate the shape of murmurs and register their dominant frequencies and relative intensities at different areas. Thus it could make clinical auscultation more precise, and that was its chief value. It provided, too, a permanent record, which was useful in follow-up, in case-to-case comparisons and for teaching purposes. Tracings showing its use were shown under the headings of congenital heart disease, the second heart sound, mitral valve disease, aortic valve disease, systolic murmur and triple rhythms.

Dr. Gardiner showed patients illustrating the use of the instrument.

The first was a man of sixty-seven years, who had been referred with a diagnosis of aortic incompetence. The phonocardiogram showed a typical "late systolic murmur". Dr. Gardiner said that that type of murmur was innocent and the results of all other tests were normal.

The second patient was a child of eleven years with mild pulmonary valve stenosis. She had a high systolic murmur and thrill at the pulmonary area, the pulmonary element of the second heart sound being delayed and rather soft. That was stated to be a common finding with mild or moderate pulmonary valve stenosis and was clearly recorded by the phonocardiogram.

The next patient was a boy of six years with typical signs of ventricular septal defect. The phonocardiogram recorded a long, loud murmur at the left sternal edge, but sharply confined to systole. By contrast the fourth patient was a mongol child of two years with a loud murmur at the left sternal edge and pulmonary area, which had been regarded as systolic. The phonocardiogram showed it to start after the first sound and to run through the second heart sound into diastole. It was thus a typical but non-continuous Gibson murmur, suggesting patent *ductus arteriosus*. Other signs led to the belief that the child had a large shunt and required operation.

The fifth patient was a woman of thirty-eight years, who presented with left inframammary pain, but no dyspnœa on exertion. She had a loud opening snap audible at the apex and within, well recorded with the phonocardiogram, but a pre-systolic murmur could be heard at the apex only with difficulty, after exercise. Electrocardiogram and X-ray findings were consistent with the diagnosis of mild mitral stenosis.

"Vascular" Scleroderma.

DR. A. J. BARNETT showed a chart with a "working" classification of scleroderma. It was divided into purely dermatological scleroderma (which was taken to include various forms in which the lesion was confined to the skin, either localized or widespread, but without vascular disturbance or visceral lesions) and "vascular" scleroderma

(which was taken as scleroderma associated with vascular disturbances, particularly Raynaud's phenomenon and ischæmia of digits). The "vascular" form was subdivided into "primary", in which the sclerodermatous changes occurred early (within one or two years of the onset of vascular phenomena), and "secondary", in which sclerodermatous changes occurred after a long history (of the order of ten to twenty years) of Raynaud's phenomenon or digital ischæmia. "Primary" vascular scleroderma could remain localized to the extremities or might become widespread, affecting the skin of other parts of the body and also internal organs. Charts were shown describing views on the ætiology of "vascular" scleroderma (collagen disease, psychosomatic disorder, primary vascular disease), symptomatology and treatment.

Four patients were shown illustrating various aspects of vascular scleroderma. The first was a man, aged sixty years, who had suffered the onset of Raynaud's phenomenon when aged fifty years, followed by two years of stiffness and swelling of the fingers. Sclerodermatous changes were localized to the fingers.

The second patient, a man, aged forty-six years, had some three and a half years previously developed Raynaud's phenomenon, followed shortly by sclerodermatous changes. Those had progressed rapidly to involve the skin of practically the whole of his body. Activity had been greatly limited because of hindrance to joint movement by the thickened skin and also by joint lesions. Marked improvement in the skin condition had occurred while the patient was under treatment with cortisone. During treatment he had developed pericarditis.

The third patient was a woman, aged forty-nine years, who had developed Raynaud's phenomenon when aged forty-four years, and later severe ischæmia of the feet with necrosis of two toes of the right foot. She had sclerodermatous changes of her hands and face, mottled opacities in the lungs, and arteriographic evidence of occlusion of large arteries.

The fourth patient, a woman, aged forty-two years, had had Raynaud's disease since childhood, with swollen stiff joints of the hands and dysphagia for two years. She had sclerodermatous changes in her hands and face, and a dilated, atonic lower third of her œsophagus. Dr. Barnett said that the last patient seemed to provide a link between the "primary" and "secondary" types of "vascular" scleroderma.

Selective Phonocardiography.

DR. MARGARET DOWN discussed selective phonocardiography. She described the physical principles which applied to this new and so far experimental form of phonocardiography, and said that it differed from the phonocardiography in general use at the present time, in that it recorded all vibrations associated with the heart's activity, rather than merely amplifying stethoscopic findings. The range of vibrations extended from the gross movement of the apex beat through a number of intense but inaudible (infrasonic) vibrations into the sonic range of 30 cycles per second, to which the ear was relatively insensitive, and up to a maximum frequency of 1000 cycles per second, to which the ear was most sensitive. The machine might be described briefly in the following way. The currents generated by a microphone placed on the chest wall were passed through a series of amplifiers and electronic filters, which separated the sound components into a series of frequency bands, each of those being recorded simultaneously in a battery of double-gun cathode ray oscilloscopes. The electrocardiogram and venous or arterial pulse waves could be recorded on the same tracing. The permanent records were made with a high-speed camera designed for cathode ray oscilloscopes.

Dr. Down said that the immediate aim in the present research project was to analyse the cardiac vibrations in normal individuals, determining (i) the component pure tone frequencies of the complex waves recorded, (ii) the time of onset of wave forms in relation to the *Q* deflection of the electrocardiogram, and (iii) the duration of each wave form.

Multiple Myeloma.

DR. DONALD DUFFY presented details of three cases. In the first the patient was a man, aged sixty-nine years, who had been treated for some months for anæmia resistant to iron and liver therapy, and as such had been referred for investigation. A blood film examination showed extensive rouleaux formation, and a sternal marrow examination disclosed the typical "myeloma cell" infiltration. X-ray films of the skeleton were devoid of changes in any way suggestive of myelomatosis, and Bence-Jones protein was absent from the urine. A satisfactory hæmoglobin level was maintained after treatment with urethane.

This case was contrasted with another in which widespread pain had been the main symptom and in which characteristic radiological changes were present in the bones together with Bence-Jones protein in the urine. Dr. Duffy pointed out the likelihood that impaired renal function would occur in patients excreting myeloma proteins in the urine.

A series of chromatographs were demonstrated, prepared from the serum and urine of patients with myelomatosis by Miss Bick, of the biochemistry department of the hospital.

Lupus Erythematosus.

The second case was that of a man, aged thirty-nine years, who had presented with a history of a pyrexial illness of three weeks' duration, which had failed to respond to assorted antibiotic administration. On the patient's admission to hospital the outstanding features were pyrexia, toxæmia, joint pain and swellings, bleeding gums and splenomegaly. Blood examination disclosed the leucocytic changes commonly found in *lupus erythematosus*; so treatment was commenced with cortisone. The patient responded satisfactorily and was back at work maintained on a daily oral cortisone dose of 75 milligrammes. However, from time to time he still suffered painful swellings of the wrists and fingers.

Acute Porphyria.

The third case was that of a woman, aged twenty-three years, who had been diagnosed four years previously as having acute porphyria, when an epileptiform convulsion and persistent abdominal pain followed appendicectomy and porphyrins were found in the urine. Improvement at that time seemed to follow treatment with cortisone; but when it was repeated during her most recent exacerbation, little response had been noted to date. Experience of another case of porphyria, in which the patient was similarly treated with cortisone, had failed to show any beneficial results from doses as high as 500 milligrammes daily.

Myeloproliferative Syndrome.

DR. JOHN MCLEAN and DR. ROSS HAYES presented a demonstration of myelofibrosis (myeloproliferative syndrome). Four patients were shown.

The first, a man, aged seventy-two years, had been admitted to the Alfred Hospital on July 10, 1953, suffering from severe leucoerythroblastic anæmia. The spleen was enlarged eight centimetres below the costal margin. Splenic puncture revealed myeloid metaplasia, and a rib biopsy showed myelofibrosis. A course of treatment with cortisone had no beneficial effect. Frequent blood transfusion was necessary, and over a period of fifteen months he had forty direct transfusions. Latterly the transfusions were required more frequently, and there was evidence of increased destruction of blood cells. On November 23, 1954, splenectomy was performed by Dr. K. Morris, using the transthoracic approach; since that date the patient had been comparatively well, and no further blood transfusions had been given.

The second patient, a man, aged fifty-four years, had been first seen in December, 1953, when he was found to have a large spleen which extended almost to the umbilicus. Blood examination showed a leucoerythroblastic type of anæmia and a rib marrow section revealed myelofibrosis. Treatment with cortisone was given, but was discontinued when symptoms of cardiac failure developed. Frequent blood transfusions were required. A course of deep X-ray therapy to the spleen (total dose 300*r*) was followed by a deterioration in his condition. Excessive destruction of red blood cells was confirmed by investigation of the fæcal stercobilinogen content, which was estimated to be 920 grammes *per centum*. Splenectomy was performed on June 21, 1954, by Dr. C. J. Officer Brown, by the transthoracic approach. Since the operation the patient's condition had improved, but he still required occasional blood transfusions.

The third patient, a man, aged sixty-six years, had been admitted to the Alfred Hospital on October 9, 1950. Blood examination had revealed an increase in blood platelets, and bone marrow examination showed an excessive number of megakaryocytes. The condition was diagnosed as megakaryocytic myelosis and myelofibrosis, and he was given a course of treatment with nitrogen mustard (total dose 29 milligrammes). That was followed by a fall in the platelet count to a normal level. Two years later his condition deteriorated, and a second course of treatment with nitrogen mustard was given. Since that time there had been two further relapses, which had been treated with triethylene melamine. At present the platelets and leucocytes were again increasing in numbers.

The last patient, a woman, aged forty-seven years, had first attended the hæmatological clinic of the hospital in

July, 1954. Enlargement of the spleen had been discovered in a routine physical examination. The edge of the spleen was palpable beyond the umbilicus. Blood examination showed a hæmoglobin value of 8·7 grammes *per centum*, a red blood cell count of 3,300,000 per cubic millimetre, a leucocyte count of 2500 per cubic millimetre and a platelet count of 130,000 per cubic millimetre. Immature neutrophile cells and normoblasts were seen in the blood film. Rib biopsy showed increase in the bone formation, and in the marrow spaces there was a cellular pattern consistent with myelofibrosis. X-ray examination of bones showed some increase in density. In that case the term myelosclerosis was considered to be a more appropriate description than in the other three cases, in which no abnormality of the bone was apparent in X-ray films.

Dr. Hayes demonstrated relevant pathological findings in the cases under consideration, together with rib biopsies and post-mortem specimens from other cases, emphasizing the wide histological variation that occurred in these conditions. He also referred to transition cases, emphasizing the lability of pathological pattern that had occurred in the natural history of those diseases which had been grouped under the heading of myeloproliferative syndrome—namely, *polycythæmia vera*, myeloid leuchæmia, megakaryocytic myelosis and myelofibrosis.

Hæmophilia and Surgical Procedures.

DR. R. SAWERS first showed two patients suffering from hæmophilia in order to demonstrate the method of controlling the hæmorrhagic state during major surgical procedures. He said that two years previously Dr. K. Jamieson had performed craniotomy on a four-year-old boy to evacuate an extensive extradural hæmatoma. Hæmorrhage was effectively controlled by large transfusions of freshly collected citrated blood given by the exchange technique at intervals of two or three days over a period of eighteen days.

More recently a man of seventy-one years had had his rectum excised by Dr. R. Officer on account of carcinoma. He was a proven hæmophilic, and his bleeding state was controlled by fresh plasma and blood transfusions up to the seventh post-operative day, from which time further treatment was not required.

Anæmia.

Dr. Sawers then showed two patients who were being treated for anæmia. An elderly woman had been treated with a preparation for oral administration supplied by a drug manufacturer and containing vitamin B_{12} and intrinsic factor. After an excellent initial response, the patient developed neurological symptoms suggesting subacute combined degeneration. No evidence of infection could be found, and after a period of observation, treatment with injections of vitamin B_{12} in 200 microgramme doses at weekly intervals was commenced; recovery rapidly occurred.

The other patient shown was a boy with pure red blood cell hypoplasia, who had received blood transfusions during the past fourteen years, at approximately three-monthly intervals, commencing at the age of three months. He now had hepato-splenomegaly, and biochemical studies indicated a moderate degree of liver disease, presumably from hæmosiderosis. He had an aminoaciduria of significant degree, but anthranilic acid could not be demonstrated. Hormone therapy, including ACTH and cortisone, administration of cobalt chloride and vitamin therapy had not influenced erythrocte generation.

Silver Wire Filigrees for Hernia Repair.

DR. LEONARD BALL demonstrated the use of silver wire filigrees for the repair of inguinal hernia. He said that the method had been in use continuously at the Alfred Hospital since 1912. He showed the method of using the filigree, the indications for its use and the method of making the filigrees.

Surgical Conditions of the Kidneys.

DR. ROBERT S. LAWSON showed a series of patients illustrating the common surgical conditions of the kidneys and their treatment. Six patients were shown after operation for renal or ureteric calculus, illustrating the various surgical approaches and procedures required in different circumstances. They included a patient with staghorn calculus, one with calculus in a horse-shoe kidney, and one with multiple renal and ureteric calculi associated with gross hydronephrosis, for whom the operation of ureteronephrectomy had been performed—the lower extremity of the ureter being severed through a second subumbilical incision. Post-operative excretion pyelograms were shown to indicate the late results of treatment on kidney function, with recovery from hydronephrosis *et cetera*.

Three patients with renal tumour were shown, all of them aged over seventy years. One had presented with simple hæmaturia, the second had had hæmaturia *plus* colic, while the third had had a massive tumour, weighing 44 ounces, without any urinary symptoms at all.

Three patients were shown to illustrate the late results of surgical treatment for tuberculous kidney. For one of them a second operation had been necessary fifteen months later to remove a caseous ureteric stump. It was therefore considered advisable to perform uretero-nephrectomy with removal of the whole length of ureter as the primary surgical treatment for unilateral ulcero-cavernous tuberculosis of the kidney. That procedure had been carried out in the two other patients shown. The long-term results of operation had been satisfactory in all of them.

Finally, a patient who had had hydatid disease of the kidney was shown. The patient had presented after an abdominal injury, and exploration was performed for suspected rupture of the spleen. The condition found at operation was an intracystic rupture of a large hydatid cyst of the left kidney—previously symptomless. A transperitoneal nephrectomy was performed from the anterior approach with a satisfactory outcome.

Paraplegia.

The neurosurgical unit presented a number of patients with spinal cord injury; some had paralysis from the waist downwards, and others had paralysis extending to the lower cervical region.

Methods of nursing with use of a rotor bed and care and management of the bowel and bladder were illustrated.

One patient was shown to demonstrate how twenty-four-hour control of the bowel and bladder could be achieved.

The physiotherapists showed a patient walking with the use of leg splints.

The value of tidal drainage and cystometry in bladder control was emphasized. In that regard a new type of tidal drainage apparatus was used, in which a rubber diaphragm had been introduced to break the syphon.

An automatic recording apparatus used in conjunction with tidal drainage enabled weekly graphs to be made in order to determine bladder contractility, volume, residual urine *et cetera*.

A plea was made for the establishment of a spinal injury centre in Victoria, so that those affected could be managed with the greatest efficiency.

Bone Grafts.

DR. JOHN CLOKE showed a series of bone grafts of various types to illustrate (i) the advisability of the early use of bone graft, and (ii) the necessity of adequate fixation of the fracture and/or bone graft.

Ophthalmic Demonstration.

DR. W. M. BOX, DR. P. H. COWAN and DR. G. MAXWELL STUBBS showed patients to demonstrate the following conditions: diskoid degeneration of the macula resulting from choroidal hæmorrhage; asteroid bodies in diabetic patients; *retinitis proliferans* in a case of Eale's disease; *retinitis pigmentosa*, optic atrophy and choroiditis in cases of syphilis, thrombosis of the inferior temporal branch of the retinal vein, congenital coloboma of the choroid, and specific choroiditis of the *retinitis pigmentosa* type.

Repair of Ruptured Abdominal Aneurysm.

DR. KENNETH N. MORRIS showed a male patient, aged seventy-one years, who when first interviewed had noticed aching pains in the abdomen for the previous three months. Two days before his admission to hospital the pain had become more severe. At that time he had a blood pressure of 145 millimetres of mercury, systolic, and 80 millimetres, diastolic, and there was a tender pulsatile mass in the abdomen above the umbilicus. The diagnosis was made of leaking abdominal aneurysm, and operation was decided upon. Whilst awaiting operation the patient suddenly became pulseless, and respiration ceased. It was apparent that he had had a catastrophic hæmorrhage from his aneurysm. Fortunately, skilled help was at hand, and intubation of the trachea, with artificial respiration and massive transfusion, restored the patient to a state in which he was able to be transported to the operating theatre. The ruptured abdominal aneurysm was excised and replaced with an aortic graft, which was joined above to the aorta just below the renal vessels, and below was anastomosed to both common iliac arteries. The patient

made a good convalescence, which was interrupted only by the appearance of a small pulmonary embolus, and a hæmatoma of the rectus sheath in the second week. He was discharged from hospital well, with good femoral pulses, in the fifth week.

X-Ray Demonstration.

DR. B. L. DEANS demonstrated X-ray films of chronic non-specific inflammatory masses which had resembled pulmonary neoplasm both clinically and radiologically. The findings were based on a pathologist's report on the specimens removed at operation. It was emphasized that, in the present state of knowledge, definite diagnosis was frequently not possible without thoracotomy.

Pathology Museum Demonstration.

The pathology museum, which had recently been rearranged, with new cupboards and new lighting, was open for inspection. Various methods of presentation of morbid anatomy specimens were shown. As well as demonstrations designed primarily for undergraduate teaching, there was an exhibit illustrating the surgical pathology of benign intrathoracic tumours.

DR. BRYAN HUDSON, DR. I. H. CUMING and MISS M. BICK showed charts of serum and urinary electrolyte changes found in patients treated for diabetic coma. Similar analyses from post-operative subjects were also shown. The assistance of Dr. K. Taylor in preparing the charts was acknowledged. The biochemistry department was open for inspection.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held in the New Medical School, Frome Road, Adelaide, on July 1, 1955.

Chlorine as a Plant Nutrient.

C. M. JOHNSON, of the University of California, Berkeley, California, presented a paper on "Chlorine as a Plant Nutrient". He said that work initiated at the University of California by P. R. Stout, C. M. Johnson, T. C. Broyer and A. B. Carlton to study the cobalt nutrition of plants had led to the conclusion that the fifteen elements usually considered adequate for the nutrition of green plants failed to provide healthy growth of tomato, sugar beet, lettuce, cabbage, carrots, alfalfa and subterranean clover. A sixteenth element, chlorine, was shown to be necessary for the proper nutrition of those plants. In the absence of adequate supplies of chlorine, as chloride ion, tomatoes wilted badly, developed a characteristic chlorosis and necrosis, grew with much reduced yield and failed to set fruit. Other plants showed similar symptoms of chloride deficiency, with symptoms which were peculiar to each species. "Kodachrome" slides of affected and normal plants were shown to illustrate these effects.

It was further stated that reduced yields were obtained when the amount of chloride supplied was less than 20 microequivalents per litre of nutrient solution. Severe foliar deficiency symptoms were seen when the supply was less than six microequivalents. The amount of chloride in chloride deficient leaf tissue was quite large, in the order of six to eight microequivalents per gramme of dry material (200 to 300 parts per million). That was much larger than the corresponding figures for molybdenum-deficient leaves (0·10 part per million), or zinc-deficient leaves (15 parts per million).

The chloride in the atmosphere, as minute aerosal particles, or in rain, could supply sufficient chloride to prevent the development of severe deficiency symptoms unless special care was taken to filter the air supply through, for example, activated carbon filters. It did not appear likely, for that reason, that chloride deficiency would be found in plants grown under natural conditions, although search was being made for areas where land to land cycled rain might provide too little chloride for optimal growth of some plants.

Reversible Effects of Heparin and Protamine on Alimentary Lipæmia.

W. D. BROWN gave a résumé of work done over a number of years on the effects of heparin in clarifying visibly lipæmic plasma *in vivo*. He said that clarification of lipæmic plasma during fat absorption was independent of the amount of fat absorbed. The opacity of the thoracic duct was not visibly altered. Clarification was associated with a decrease in chylomicron count and total plasma fat. In certain circumstances the decrease in total lipid was associated with a transitory increase in invisible lipids. Those effects were complete within several minutes of heparinization. Alimentary lipæmia did not occur in heavily heparinized rats fed neutral oil.

Other workers had shown that "clearing factor" produced by heparin *in vivo* would clarify turbid plasma *in vitro*. It appeared therefore that heparinization led to a redistribution of lipid and protein in plasma followed by a rapid loss of certain lipid constituents from the blood-stream.

Protamine promptly reversed the antilipæmic effects of heparin in fat-absorbing rats and dogs. It also increased alimentary lipæmia in otherwise untreated rats. That observation was the first evidence that heparin synthesized *in vivo* might be a factor regulating fat transport in the body. Protamine and heparin were mutually antagonistic in their effects on alimentary lipæmia. The evidence from all published sources suggested that "clearing factor" was a complicated enzyme system, and protamine appeared to act simply as an inhibitor of heparin, the latter both stimulating the production of the system and intervening in its action as a prosthetic group. The anticoagulant dextran sulphate had some heparin-like properties on alimentary lipæmia.

Effects of heparin on the endogenous lipæmia of pregnancy in the rat were studied. The striking action of heparin in abolishing that lipæmia was not shared by dextran sulphate. No simple correlation between anticoagulant and antilipæmic effects was found. However, a precipitate formed in the plasma drawn from the rats after treatment with either anticoagulant. It was now known that that indicated that both anticoagulants produced the lipase component of the clearing factor system. There was some evidence that a similar precipitate formed in small quantities *in vitro* in normal sera from rats with the endogenous lipæmia of pregnancy. Protamine had no effect on that lipæmia *in vivo*.

The albumin character of the interfacial protein of chylomicrons in lymph was confirmed, and it was found that protamine *in vitro* flocculated chylomicrons above pH 4·7. In some cases an unusual clotting phenomenon occurred which involved a surface reaction on the chylomicrons. That phenomenon was unexplained. Flocculation of chylomicrons, followed by filtration or low-speed centrifugation, separated chylomicrons from normal or thrombin-treated chyle, and it was proposed as a routine procedure for that purpose.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

EARLY EXPLORATION.[1]

[From the diary of Joseph Arnold, M.D., F.L.S., July 13, 1815.]

EVEN Mr. Evans who went 150 miles south west of Bathurst Plains has not been sufficiently rewarded and is now going down the Derwent to his wife and family. The large river that Mr. Evans discovered flowing to the south west it is supposed will fall into the sea somewhere about Bass' Straits. Mr. Evans told me the banks were very strait and lofty as if it were subject to inundations: vast quantities of emus, kangaroos, and water moles were seen. The fish in the river he describes as very large. Most of the country was covered by a saccharine matter which resembled manna: it appears in small drops or tears of various sizes, and is of a more pleasant taste than manna. Some that Mrs. Molle gave me to taste of at the Governors table, tasted very much like the sugar that is covered over wedding cakes. Mr. Evans said that he thought one person could collect about a gallon of it in a day and that he used to eat a great deal of it in his travels. It is equally found on the ground, stones, and plants, so that it cannot be an exudation from any vegetable. I am induced to believe that it is the production of an insect of the Gryllus tribe which is either excrementitious or an article of food.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

ULTRA-VIOLET RAYS.

SIR: There has been an increase of therapeutic use of physical agents over the last few years and advancement of knowledge gained therefrom, which makes one speculate as to what further use will be found in the future. Prominent among the agents that is of great interest, but of which we understand little of its complex workers, is ultra-violet radiation. There is a variety of effects of ultra-violet radiation, and various zones of the large field of the spectrum cause different biological responses, the principles of which are still for the most part unsolved.

The antirhachitic effect, in which the rays between 2800 and 3200 Ångström units cause in the skin an activation of cholesterol to form vitamin *D*, which is so important in the calcium and phosphorus absorption by the body, is an example.

Probably of equal importance is the bactericidal effect in which the wave-lengths of around 2500 to 2650 Ångströms are the most effective. Ultra-violet rays have been used for some years now on the skin surface. Growing use of them is also being made commercially—for example, air and water sterilization.

The mention of this artificial sterilization causes us to reflect upon the bactericidal process that goes on in those places where microorganisms are exposed to the sun's rays. Thoughts along these lines lead one to wonder, in a very speculative manner, whether ultra-violet rays could be used with some added advantage in the preparation of vaccines, including that for anterior poliomyelitis.

Yours, etc.,

Sydney, "HELIOS".
October 26, 1955.

THE PLENARY SESSION ON CANCER AT THE RECENT CONGRESS.

SIR: Since I had no right of reply at the time, I wish to reply now to Sir Stanford Cade's remarks (in reply to the discussion) at the plenary session on cancer in the recent Australasian Medical Congress in Sydney last August.

Much of what he said (which I wrote down at the time) has been omitted from pages 528 and 529 of the October 1 issue of THE MEDICAL JOURNAL OF AUSTRALIA. He commenced by saying: "Dr. Belisario has mentioned the use of splenic extract, podophyllin and carbon dioxide snow. On these I will not comment. But I will comment on his attempt to disparage members of other branches of the medical profession because no specialty has the monopoly of making or not making mistakes." Here, as throughout his remarks about me, he either misinterpreted and/or misrepresented what I had said. In relation to the above I stated: "There should be cooperation between the surgeon, the radiotherapist and the dermatologist, in the care of cutaneous malignancies. The dermatologist, by the very nature of his specialty, should be best qualified to diagnose skin lesions and to judge between the forms of treatment applicable."

I think any fair-minded person cannot but agree that it would be just as irrational to expect a radiotherapist or surgeon to be as proficient as a dermatologist in the diagnosis and management of cutaneous lesions (including early cancers) as it would be to expect a dermatologist to be proficient in diagnosis and treatment in their respective fields.

I made no suggestion, as Sir Stanford inferred, that dermatologists do not make mistakes, but I do contend that a well-trained, experienced dermatologist should make fewer mistakes in his own field than a radiotherapist or a surgeon in the dermatological field. It was for this reason that I stressed the need for cooperation between the three (a cooperation with which Professor Windeyer agrees and has advocated in writing) in the management of cutaneous malignancies. In this way the best treatment is selected for all cases, whether surgical, dermatological or soft or hard X- or radium radiation.

I mentioned one of many examples of what could happen in the absence of such cooperation: a case of sporotrichosis sent by a general practitioner to a radiotherapist for treatment of the tumours on his arm and hand caused by this mycotic infection which is radioresistant. The tumours cleared up quickly after dermatological consultation when iodides were given by mouth. Here Sir Stanford Cade himself showed how great is the need for cooperation with the dermatologist, because he said: "I would prefer it if the rare disease—the gumma—was missed by a radiotherapist rather than that the commoner condition—skin cancer—should be missed by a dermatologist." Such a remark would indicate that because I had mentioned a tumour disappearing with iodides I must have been talking about a gumma, and that he knew nothing of sporotrichosis, its diagnosis and treatment. Again, in stating, as he actually did at the time, that "he would much prefer to see a gumma missed by a radiotherapist than lots of skin cancers missed by dermatologists", one can realize that he considered dermatologists have very little knowledge concerning the diagnosis of skin cancer. This indicates a very real lack of knowledge on his part of Australian conditions where skin cancers are ten times as common as in Great Britain (Molesworth, E. H., 1944, "An Introduction to Dermatology", J. and A. Churchill, Limited, London, page 441, line 5, last paragraph). Consequently it ill behoves Sir Stanford Cade to disparage the diagnostic or therapeutic ability of the experienced dermatologists in this country, since the management of cutaneous carcinomata forms a larger part of the practice of most Australian dermatologists than that of other members of the medical profession.

Despite what appears on page 529 of the journal, in my opinion and that of many others who spoke to me, Sir Stanford, not content with his previous statement, implied, if he did not actually say, that I advocated or actually acquired a vested interest in patients which could or did conflict with the best interest of the patients themselves. Also he likened some of the types of treatment advocated by me to a manual trade and added: "Let us get away from a trade and back to medicine."

I stated on page 528 that "fortunately there was already full collaboration in New South Wales" (between the surgeon, radiotherapist and dermatologist) and merely advocated that such collaboration should become world-wide, which it is not at present—*vide* Queensland and England as examples where the dermatologist is mostly by-passed when early cutaneous carcinomata are concerned (Goldsmith, W. N., and Hellier, F. F., 1954, "Recent Advances in Dermatology", J. and A. Churchill, Limited, London, page 353, line 15).

Judging by the opinion of large numbers of the members who were present at this plenary session, and who came up and spoke to me or rang me up afterwards, I was not the only one who was surprised at the tone of Sir Stanford Cade's remarks.

Yours, etc.,

Harley, J. C. BELISARIO.
143 Macquarie Street,
Sydney.
October 10, 1955.

MEDICAL HISTORY OF THE WOLLONGONG DISTRICT.

SIR: In your edition of October 29 Dr. Kirkwood draws attention to a mistake of mine. He worked with me as my assistant till he left to go to World War I. When he returned with a Military Cross I offered him a junior partnership with me at Port Kembla. As the years went by I found that the Wollongong end of the practice was increasing so much faster than the Port Kembla end that I asked him to join me in Wollongong. A very happy association lasted for eleven years, when, owing to his increasing deafness, he relinquished general practice. I apologize for my error which I think he himself describes as trivial.

Yours, etc.,

Wollongong, HARRY H. LEE.
New South Wales,
Undated.

P.S.—I do not ever remember being called "Young Harry", but always "Young Arry".

THE PENSIONER MEDICAL SERVICE.

SIR: I wonder if Dr. H. C. Colville would care to state his reasons for having the pensioners' payment vouchers transferred from the doctor to the patient. Dr. J. F. Harley rightly denounces it in the absence of reasons being stated for its adoption, and he quotes good reasons for maintaining the *status quo*.

There are other reasons, too. If the hygienic condition of some of the patients' cards at present are any indication of the future condition of our vouchers, we shall require a special receptacle for them. And what about the young ladies of the Health Department who have to count the vouchers and stamp them? Has Dr. Colville seen this being done? The speed achieved at present with clean vouchers will be sadly disturbed by vouchers which are dog-eared, torn, and perhaps in some odd cases adhering together with bacon and egg, chewing gum and an odd tuberculous sputum. Has the proposal been subjected to their trade union?

Yours, etc.,

133 Wigram Road, JOHN A. McCLUSKIE.
Glebe,
New South Wales.
November 4, 1955.

A SYNDROME OF CONGENITAL ABNORMALITIES.

SIR: We would like to draw attention to a syndrome of congenital abnormalities which has recently come to our notice. During the past year we have examined four infants in whom the usual site of the clitoris was occupied by a flap of skin-covered tissue approximately two centimetres in length, about one and a half centimetres in width and about one centimetre thick. No other abnormality of the vulva was noted. All these infants had a characteristic facies which might possibly be described as "sprite-like", and three of them suffered from various associated congenital abnormalities, which included syndactyly of toes, talipes, bony abnormalities preventing full extension of the elbow joints, limitation of extension at the metacarpophalangeal joints, and a localized defect of scalp tissue. We would be very interested to hear of any similar cases which may have come to the notice of your readers.

Yours, etc.,

ROBERT VINES,
LORIMER DODS.
The Institute of Child Health,
Royal Alexandra Hospital for Children,
Camperdown,
Sydney.
November 7, 1955.

THE DEVELOPMENT OF MODERN PSYCHIATRY IN RELATION TO MEDICINE AND SURGERY.

SIR: Dr. Rudduck's Stawell Prize Essay (M. J. AUSTRALIA, October 29, 1955) stands out as a contribution reflecting exactly the sort of approach to the problems of medicine which Sir Richard himself enjoined and demonstrated. I well remember a clinical aporism of Stawell's to us students: "We must seek a broad philosophical approach to clinical problems." Dr. Rudduck's essay is all that; and it is free from that common pitfall of philosophy—divorce between theory and practice—which it would seem likely led Plato to hold that the physician should not be a philosopher.

A special merit, to my mind, of Dr. Rudduck's article is that in it, instead of emphasizing the usual terminology about "the unconscious" (a psychic category) he stresses the fact of "impressed neurons" (a physical category). The conventional discussion about (to put it starkly) "the unconscious consciousness" involves a contradiction in terms which is logically untenable; but when the fact (itself indubitable) that past and forgotten experiences influence present thought, feeling and conduct, is explained in terms of some permanent physical change in the nervous system, the explanation is simple, comprehensible and convincing. No one would seek to explain the recurring disharmony produced at a certain place in the playing of a gramophone record by involving some mystical, inaudible discord of a previous occasion—inaudible like the music of the spheres, but affecting the now audible music. One says, simply, it is due to a scratch on the record, itself a medium designed, when energy is played into it in a special sort of way, to turn out that energy in harmonic vibrations. So also the nervous system. Of course, we are still left with the mystery of the nature of relation between "impressed" nerve cell activity and consciousness.

One sentence in this well stated and well reasoned essay calls, I venture to think, for more and exact discrimination. Dr. Rudduck seems to commit himself to a particular metaphysical explanation which, closely examined, has proved unacceptable to many careful thinkers both scientific and philosophical.

In the sentence referred to Dr. Rudduck seems to identify (as contrasted with interdependence, the one with the other) conscious processes and neurological happenings. To quote: "One cannot yet determine how the brain reaches awareness . . . a probable explanation is that a still higher arc [apparently a neurological arc superimposed on Cajal's six neuronic arcs] may have been evolved. *This arc may include afferent and efferent thoughts.*" (Italics mine.)

Considering the admitted amazing and baffling interdependence of brain working and mental process, it may appear pedantic and obscurantist to question an assumption of identity similar to the identity, under various forms, of physical energy, such as heat and movement, but two considerations to the contrary are weighty: (i) This assumption has been specifically rejected by leading informed authorities in neurology and in philosophy—for example, Sherrington and Adrian, and the philosophers Bergson and Ayer. *Vide* my article "Brain and Mind" (M. J. AUSTRALIA, April 16, 1955). (ii) In spite of apparent remoteness from a work-a-day world, a metaphysical theory may have incalculable consequences for good or evil and for the total human situation. Witness the paramount importance of Marx metaphysical theory of dialectic materialism in giving appeal and drive to Communist practice.

Again with great appreciation of Dr. Rudduck's valuable contribution,

Yours, etc.,

CHAS. I. McLAREN.
Melbourne,
November 8, 1955.

ADVERTISEMENTS AND SAMPLES FROM DRUG HOUSES.

SIR: Recently a sample of an antihistamine was received at my home. The sample was recovered from the post by my two infant sons, who consumed, between them, 18 of the 20 sample twenty-milligramme dragees. As reference to the literature showed that there had been some fatal cases with overdosage of such preparation, the children were subjected to stomach washouts and observation, and fortunately there were no ill-effects.

While admitting negligence on the part of my household, it is thought that, had the sample packet not been of such flimsy cardboard construction and if the phial had not been so loosely stoppered with an inefficient plastic cork, this occurrence may not have happened.

I wonder if any of my colleagues have had similar worrying experiences, for, as you know, the mail is flooded with numerous samples these days. If so, perhaps an approach could be made to the drug houses and agents that specimens of samples be first submitted to a special subcommittee of the Association, who could approve or not the dispatch of them to the profession.

Yours, etc.,

November 3, 1955. MEDICAL PRACTITIONER.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

COURSES TO BE CONDUCTED IN MELBOURNE IN 1956.

THE following schedule is published as a guide for those who may be planning post-graduate study in Melbourne in 1956.

Courses for Higher Qualifications.

Part I Courses.

For candidates for Part I of the M.D., M.S., D.G.O., D.O., D.L.O., D.P.M., D.D.R., D.T.R. and D.A., Primary F.R.A.C.S. and Part I of the Diploma of the College of Radiologists, courses will be held in the following subjects.

Anatomy.—A course in anatomy commences on February 27 and will be conducted on Monday and Wednesday afternoons for four or five months.

Physiology.—A course in physiology commences on February 27 and will be conducted on Monday and Wednesday afternoons for four to five months.

Pathology.—A course in pathology commences on February 27 and will be conducted on Monday and Wednesday afternoons for four months.

Physics.—A course in physics commences on March 1 and will be conducted on Thursday afternoons for eighteen weeks.

Microbiology.—A course in microbiology commences on May 15 and will be conducted on Tuesday afternoons for thirteen to fifteen weeks.

Psychology I.—A course in psychology I commences in March and will be conducted on a part-time basis for eight months.

Part II Courses.

Course in Medicine.—A course in medicine suitable for candidates for M.D., M.R.A.C.P. will commence on June 4 and continue on a part-time basis for eight weeks at the Royal Melbourne Hospital.

Course in Surgery.—A course in surgery suitable for candidates for M.S. and F.R.A.C.S. will commence on March 5 and continue on five half-days a week for eight weeks at the Alfred Hospital.

Basic Courses for the Diplomas.—A course in microbiology will commence on May 15 and continue on Tuesday afternoons for thirteen to fifteen weeks. A course in basic pathology will commence on February 27 and continue on Monday and Wednesday afternoons for four months.

Course in Radiodiagnosis.—A course in radiodiagnosis for D.D.R. and Part II of the Diploma of the College of Radiologists will commence in May and continue on a part-time basis for ten weeks, and a course in special pathology will commence in June and continue on a part-time basis for six weeks.

Courses in Radiotherapy and Physics.—Courses in radiotherapy and physics for D.T.R. and Part II of the Diploma of the College of Radiologists will be arranged when candidates present themselves.

Courses for D.P.M.—A course in psychiatry will commence in early June on a part-time basis. Lectures will also be arranged in neuropathology. A course in psychopathology runs from March for eight months on a part-time basis.

Courses for D.L.O.—Courses in laryngology and otology and in special pathology will commence in early May and continue on a part-time basis for three to four months.

Courses for D.O.—Ophthalmology and special pathology courses will commence in early April and continue on a part-time basis for four to five months.

Courses for D.G.O.—Gynæcology and obstetrics and special pathology courses will be arranged when sufficient candidates present themselves.

Courses for D.A.—Courses in the theory and practice of anæsthetics and in internal medicine will also be arranged when candidates present themselves.

Refresher Courses.

Gynæcology and Obstetrics for Recent Graduates.—A gynæcology and obstetrics refresher course for recent graduates will be conducted at the Royal Women's Hospital, Melbourne, on a full-time basis for two weeks commencing February 6.

Pædiatrics.—A course for recent graduates in pædiatric conditions in general practice will be conducted at the Royal Children's Hospital, Melbourne, on a full-time basis for one week, commencing February 20.

Gynæcology and Obstetrics for Recent Graduates.—A gynæcology and obstetrics refresher course for general practitioners will be conducted at the Royal Women's Hospital on a full-time basis for two weeks, commencing September 3.

Medicine and Surgery.—A medical and surgical refresher course for general practitioners will be conducted at metropolitan hospitals on a full-time basis for one week commencing September 17.

Psychiatry.—A psychiatry course will be conducted by the Mental Hygiene Department on a part-time basis, commencing in March or April.

Arrangements for Conducting Courses.

Courses in medicine and surgery as set out above will be conducted by the honorary staffs of the Royal Melbourne and Alfred Hospitals respectively. The Ophthalmological Society of Australia (British Medical Association) will conduct the ophthalmology and special pathology course. The Ear, Nose and Throat Section of the British Medical Association will conduct the course in laryngology, otology and pathology for the D.L.O. Part II. The Australasian Association of Psychiatrists will conduct the course in psychiatry for the diploma, and the University of Melbourne will conduct the courses in psychology and psychopathology. The Mental Hygiene Department will conduct the psychiatry refresher course. All other courses shown will be conducted by the Melbourne Medical Post-Graduate Committee.

Enrolments.

Enrolments for all courses should be made through the Melbourne Medical Post-Graduate Committee, except those for psychology I and psychopathology, which are made with the Registrar, University of Melbourne, and for the psychiatry refresher course, which are made with the Mental Hygiene Department. The Director of the Post-Graduate Committee will be pleased to answer inquiries concerning the 1956 programme. Correspondence should be addressed to him at the Post-Graduate Committee's office, 394 Albert Street, East Melbourne.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 54, of October 27, 1955.

CITIZEN NAVAL FORCES OF THE COMMONWEALTH.

Royal Australian Naval Reserve.

Appointment.—Colin Alfred Cameron Galbraith (Surgeon Lieutenant-Commander, Royal Australian Naval Volunteer Reserve) is appointed Surgeon Lieutenant-Commander, with seniority in rank of 16th November, 1952, dated 19th September, 1955.

AUSTRALIAN MILITARY FORCES.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—The provisional rank of 1/39022 Captain P. J. Landy is confirmed. 1/33136 Honorary Captain K. F. Brady is appointed from the Reserve of Officers, and to be Captain (provisionally), 22nd August, 1955.

Southern Command.

Royal Australian Army Medical Corps (Medical).—3/63671 Lieutenant-Colonel K. H. Heard is appointed from the Reserve of Officers, is appointed Deputy Director-General of Medical Services, Army Headquarters, and to be Temporary Colonel, 1st September, 1955.

Central Command.

Royal Australian Army Medical Corps (Medical).—4/32049 Captain J. B. Murchland is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Central Command), 13th September, 1955.

Tasmania Command.

Royal Australian Army Medical Corps (Medical).—6/15206 Honorary Captain D. J. Walters is appointed from the Reserve of Officers, and to be Captain (provisionally), 9th September, 1955. 6/9310 Major A. O. Green is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Tasmania Command), 26th August, 1955.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

Northern Command.—To be Honorary Captain, 21st September, 1955: Stanley Forster McCullagh.

Eastern Command.—To be Honorary Captains, 26th September, 1955: Frank Fisher and John Francis Kemp.

Obituary.

LUDOVIC BRUNO ROSLEIGH.

WE have received from Dr. T. F. Rose the following appreciation of the late Ludovic Bruno Rosleigh.

It is with sadness that one records the passing of Ludovic Bruno Rosleigh, M.D. of Vienna, on October 15, 1955, at the age of sixty-three years.

Ludovic Bruno Rosleigh was born in 1892 in Krakow (Poland), where he started his medical studies in 1910. As a medical student he became a tutor in physiology. In the 1914-1918 war he served in the Austrian army. He graduated M.D. at the University of Vienna in 1915, joined the free Polish army and volunteered for service during the war with the Soviets in 1920; during this war he was decorated for bravery. After the war he went to Vienna to work under Professor Wenckebach, specializing in diseases of the heart. He then returned to Poland, where he remained in private practice until the 1939 war. During this time he took an active part in scientific work, lectured at a post-graduate school and published several papers in Polish medical journals. With the outbreak of the 1939 war he joined the Polish army and soon was wounded, an event which eventually led to his blindness. He was interned in a prisoner-of-war camp in Rumania, but escaped and joined the free Polish army in France. After the collapse of France he went with the army to England and came under British command. However, he soon developed sympathetic ophthalmia, and in spite of the treatment of Sir Stewart Duke-Elder he became blind in 1942. He was then accepted into St. Dunstan's and went through all his studies to become a Member of the Chartered Society of Physiotherapy, eventually setting up a practice in Wimpole Street, He was a member of the British Medical Association in London until his arrival in Australia in 1948. In Sydney he was a member of the Australian Physiotherapy Association and an associate member of the Blind Soldiers' Club. He practised as a physiotherapist in Macquarie Street from 1949 to the time of his death. His widow and his son are both practising medicine in Sydney.

Every now and then, one is privileged to be the friend of a truly great man, a man of unconquerable courage and fortitude, and such a man was Ludovic Rosleigh, who, in spite of being a cardiologist of renown in his native Poland, seized the opportunity twice to fight for the freedom of his native land—in 1920, when he was decorated for bravery, and in 1939 against Germany. During this latter war he became a prisoner in Rumania, but escaped to France and later England. Here he practised his beloved medicine, and became a member of the British Medical Association. Tragically in 1942, an old wound caused his total blindness. To many this would have meant the end of a career. For Ludovic Rosleigh, however, it meant merely the closing of one and the commencement of another. With the aid of St. Dunstan's, he became a physiotherapist and practised both in Wimpole Street, London, and Macquarie Street, Sydney, with great success despite his handicap.

It was a privilege to know this indomitable man, whose courage never faltered, and who never complained of his blindness. Even when he suffered from his coronary occlusion, he did not allow it to interfere, except briefly, with his work. Australia will be fortunate if more of the men of the calibre of Ludovic Rosleigh come to this land, bringing with them his sterling qualities of character and splendid determination to overcome all obstacles.

The Royal Australasian College of Physicians.

EXAMINATION FOR MEMBERSHIP.

INTENDING CANDIDATES for the examination for membership of The Royal Australasian College of Physicians to be held in May-June, 1955, are reminded that applications for this examination close on Friday, April 6, 1956. Application forms may be obtained from the Honorary Secretary, 145 Macquarie Street, Sydney.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED OCTOBER 29, 1955.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	2(1)	8(2)	..	..	..	..	..	10
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	1	..	..	..	..	..	..	..	1
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	1	1	..	..	..	..	..	..	2
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	6(3)	13(10)	1(1)	..	..	..	..	5	25
Diphtheria	..	7(7)	1	1(1)	12(10)	1	..	..	22
Dysentery (Bacillary)	..	4(3)	1(1)	2(2)	1(1)	1	..	..	9
Encephalitis	2	1(1)	..	1(1)	..	..	..	..	4
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	1	..	..	1
Infective Hepatitis	47(27)	95(64)	..	18(9)	4(4)	2	..	..	166
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	1(1)	..	..	..	..	..	..	1
Meningococcal Infection	6(2)	3	..	..	..	..	..	..	9
Ophthalmia	..	..	..	..	2(1)	..	..	..	2
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	..	1	7(4)	..	..	..	..	9
Puerperal Fever	1(1)	..	..	..	..	..	..	..	1
Rubella	..	89(71)	..	10(7)	2(2)	1	..	..	102
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	20(11)	28(18)	14(6)	5(3)	1(1)	..	..	..	68
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	2(1)	..	..	..	..	..	2
Trachoma	..	..	..	..	16	..	..	..	16
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	40(22)	16(9)	5(3)	10(6)	11(9)	5(3)	..	..	87
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	2	..	..	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

The written examination will take place in capital cities where candidates are offering on Thursday, May 3, 1956. The clinical examination will take place in Melbourne on or about Monday, June 11, 1956. Only those candidates whose answers in the written examination have attained a satisfactory standard will be asked by the Censor-in-Chief to proceed to the clinical examination.

Notice.

CENTENARY CELEBRATIONS OF THE ROYAL WOMEN'S HOSPITAL, MELBOURNE.

THE centenary of the Royal Women's Hospital, Melbourne, occurs in 1956. As part of the centenary celebrations it has been decided to hold a week of scientific meetings at the hospital. Subjects for discussion are to include maternal and fœtal mortality, infertility, ante-partum hæmorrhage, cancer, and puerperal and post-abortal sepsis. There will be demonstrations on obstetrical and gynæcological pathology and radiology, palliative surgery in genital cancer, the use of the "Isolette" in the care of the premature baby and relaxation training for ante-natal patients.

Professor Andrew Claye, the Sims Black travelling professor for 1956, is to be guest professor in the Royal Women's Hospital for one month of the period of his stay in Australia. He will take an active part in the discussions on papers to be presented at the meetings and will also deliver the Arthur Wilson Memorial Lecture.

LAENNEC SOCIETY.

A CLINICAL MEETING of the Laennec Society will be held at the Royal North Shore Hospital in the thoracic block at 8 p.m. on Monday, December 12, 1955. Members and others who may be interested are invited to attend and to inspect the new thoracic block prior to the meeting.

SUMMER CAMPS FOR DIABETIC CHILDREN.

THE summer camp for diabetic children for 1956 will be held at the Fairbridge Farm School, Molong, from Saturday, January 7, to Saturday, January 21. Trained staff, consisting of nurses, dietitians and school teachers, will care for the children, whose ages range between six and twelve years. Applications are invited for children attending country hospitals and for those attending private practitioners. Children attending private doctors will be charged for at the rate of £12 per week, to cover the cost of fares, accommodation, pocket money and supervision. It will probably be possible to lower this rate if the doctor in charge of the child makes a recommendation to this effect. Children attending hospital clinics are not charged for, although parents are asked to make a small contribution, which may be only fares and pocket money. Application forms may be obtained from the Honorary Secretary, Miss A. G. Allen, c.o. Dietitian's Office, Royal North Shore Hospital, Crow's Nest, New South Wales.

Deaths.

THE following deaths have been announced:

SHELTON.—Percy Gerald Shelton, on October 30, 1955, at Melbourne, Victoria.

DEVINE.—John Berchmans Devine, on October 31, 1955, at Melbourne, Victoria.

HAMILTON.—Marie Montgomerie Hamilton, on November 2, 1955, at Sydney, New South Wales.

GRIMWADE.—Sir Russell Grimwade, a complimentary member of the British Medical Association, on November 2, 1955, at Melbourne, Victoria.

KAHLA.—Sydney Ernest Louis Kahla, on November 4, 1955, at Sydney, New South Wales.

LAIDLEY.—John Walwyn Shepheard Laidley, on November 7, 1955, at Sydney, New South Wales.

Medical Appointments.

Dr. R. L. Jones has been appointed visiting surgeon to Goulburn Training Centre in the Department of the Attorney-General and of Justice, New South Wales.

Dr. P. M. Daniels has been appointed senior registrar in anæsthesia at the Royal Adelaide Hospital.

Diary for the Month.

Nov. 22.—New South Wales Branch, B.M.A.: Ethics Committee
Nov. 23.—Victorian Branch, B.M.A.: Branch Council.
Nov. 24.—New South Wales Branch, B.M.A.: Branch Meeting.
DEC. 1.—New South Wales Branch, B.M.A.: Clinical Meeting.
DEC. 6.—New South Wales Branch, B.M.A.: Organization and Science Committee.
DEC. 7.—Western Australian Branch, B.M.A.: Branch Council.
DEC. 7.—Victorian Branch, B.M.A.: Branch Meeting.
DEC. 7.—Victorian Branch, B.M.A.: Branch Council.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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